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Anaesthesia

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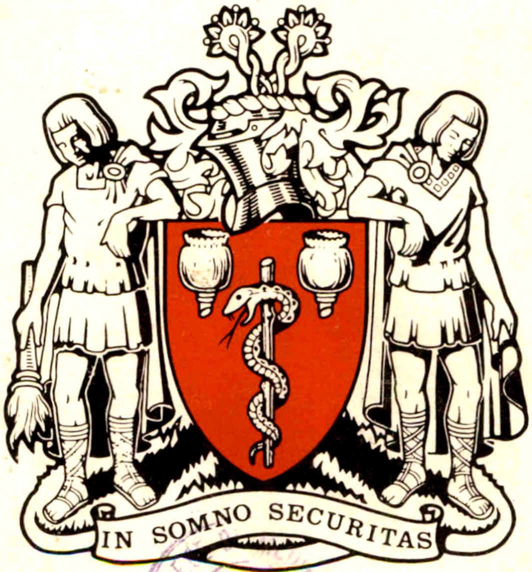

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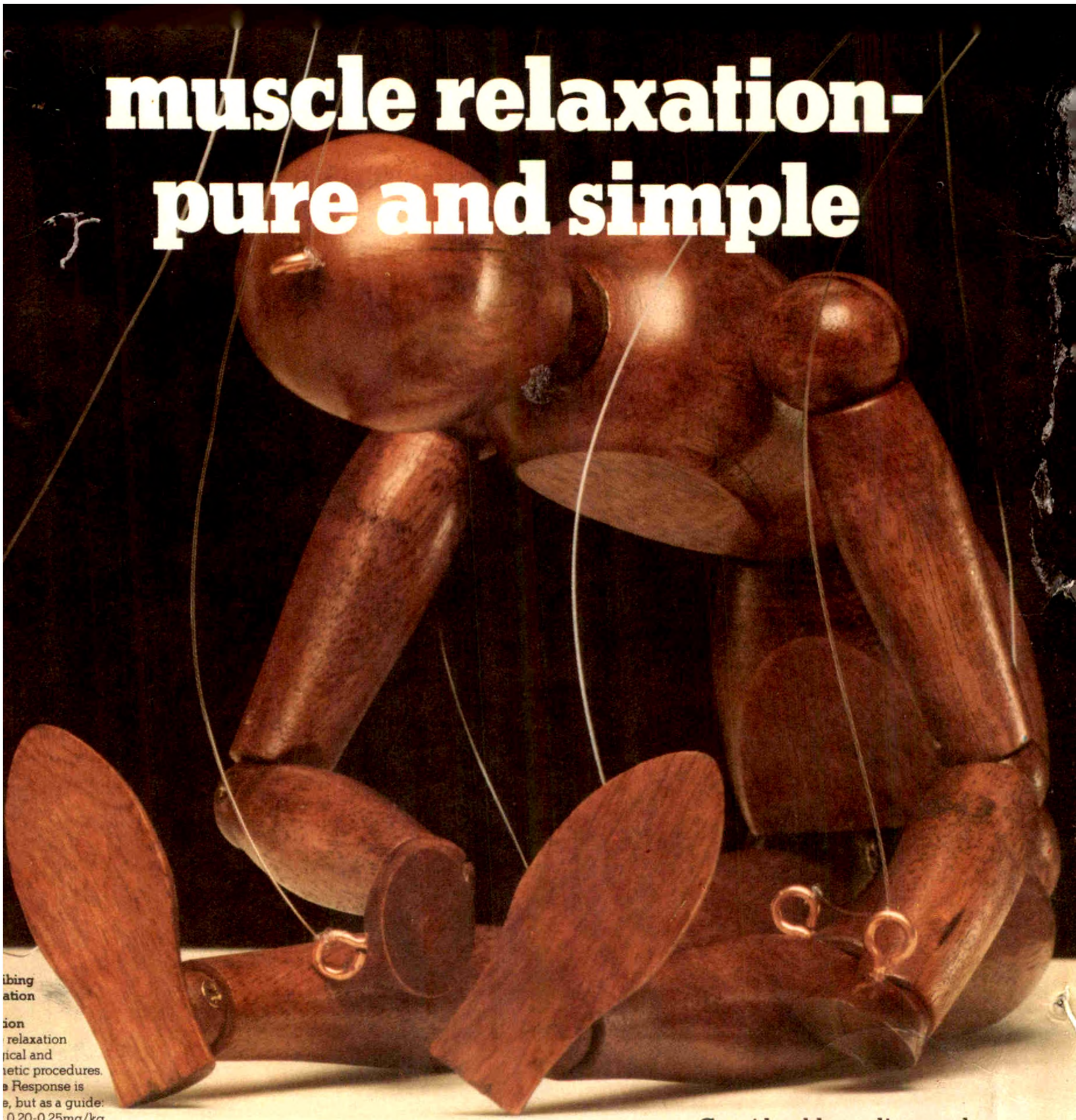

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'kg bodyweight. **Contra-indications**
ensitivity to alcuronium, myasthenia
myasthenic (Eaton-Lambert) syndrome.
tions Dosage requirements may be
in renal impairment, hepatic and
uscular diseases, and by concomitant use
iotics of the polymixin and
lycoside groups, volatile anaesthetics,
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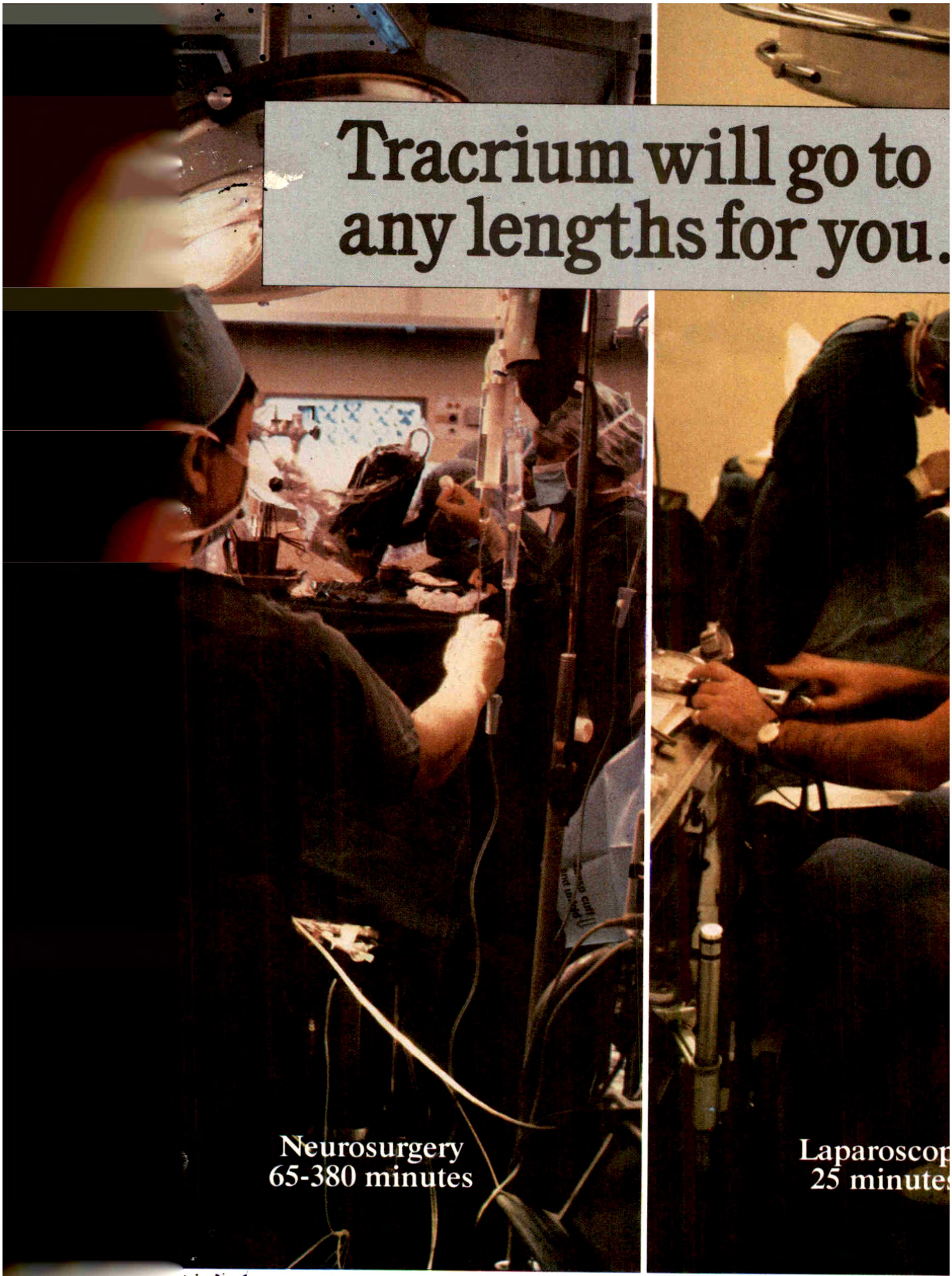

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Contra-indications, warnings, etc. Contra-indicated in patients hypersensitive to atracurium besylate. Tracrium should be used with caution in patients receiving aminoglycosides or polypeptide antibiotics and in patients with myasthenia gravis. In common with all other neuromuscular blocking agents, adequate facilities must be available for endotracheal intubation and artificial ventilation. The neuromuscular block produced by Tracrium may be increased by the concomitant use of inhalational anaesthetics such as halothane. Tracrium should not be mixed in the same syringe with any other agent; in particular it must not be mixed with thiopentone or any alkaline agent, as the high pH would cause inactivation of the Tracrium. As with all other neuromuscular blocking agents the possibility of transient hypotension due to histamine release cannot be excluded. Although animal studies have indicated that Tracrium has no adverse effects on foetal development, nevertheless, like all neuromuscular blocking agents, it should be used with caution in pregnant women. Tracrium may be used to maintain neuromuscular relaxation in Caesarean section as atracurium does not cross the placenta in clinically significant amounts.

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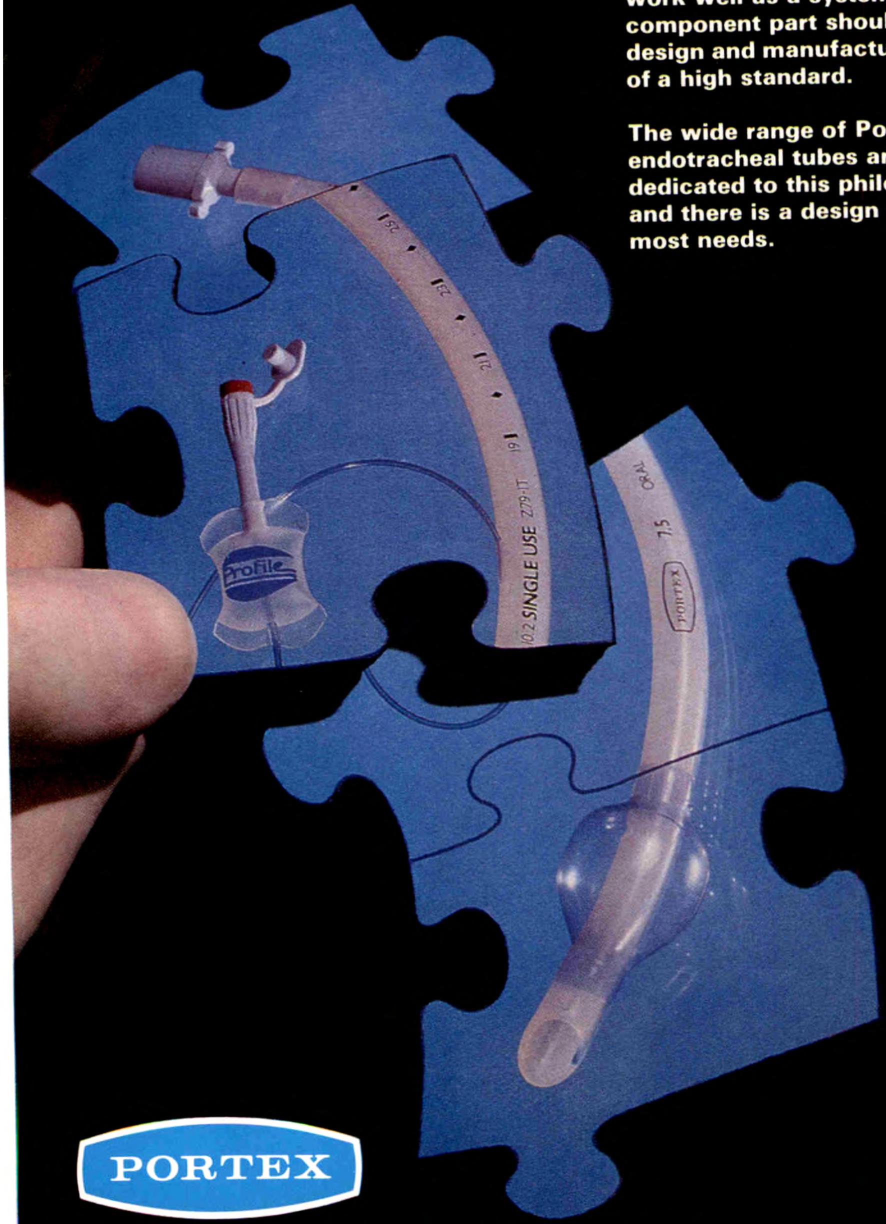

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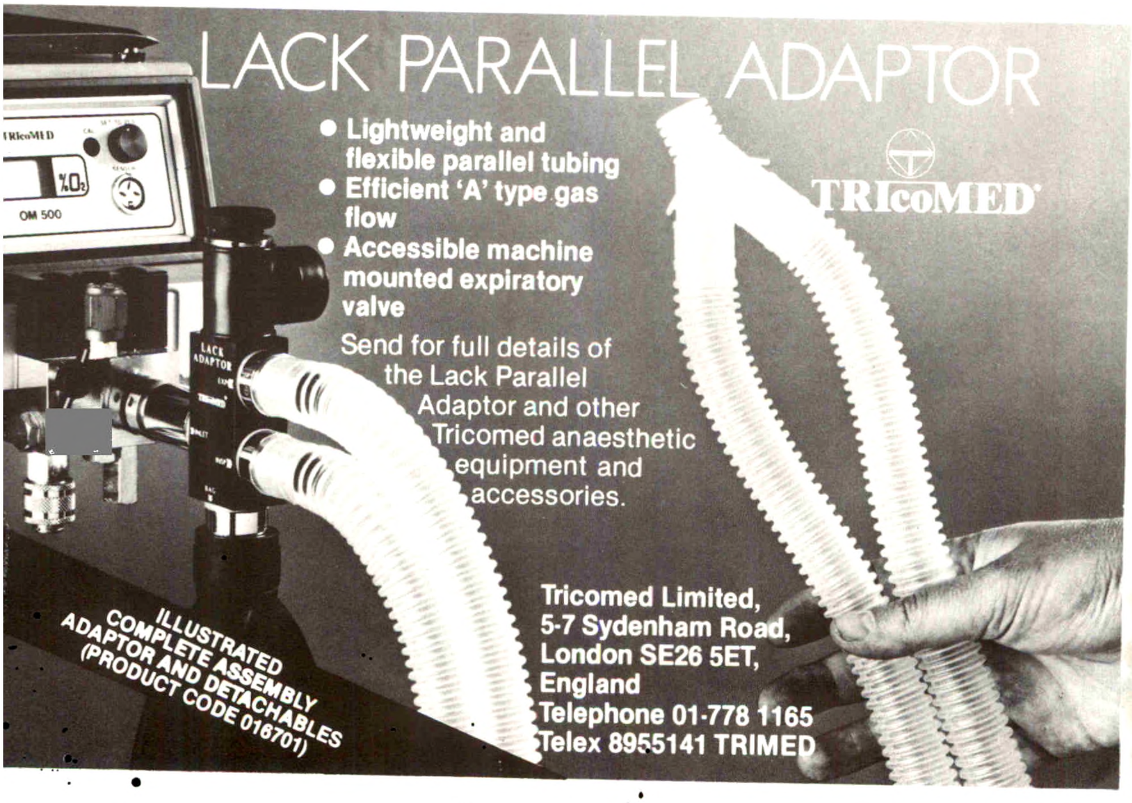

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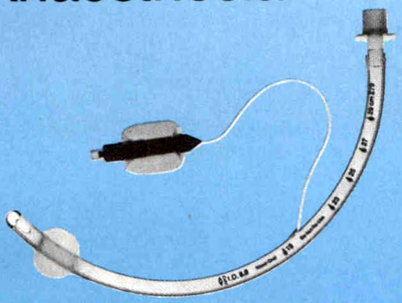

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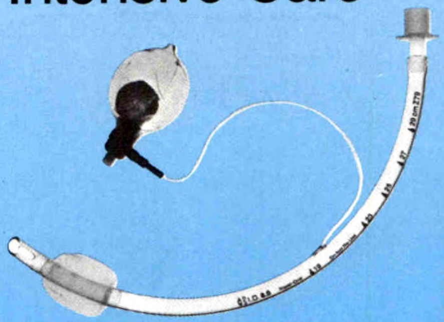

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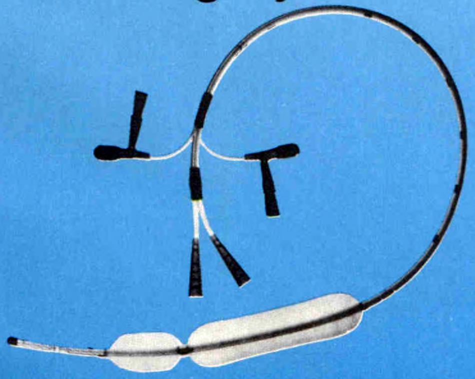

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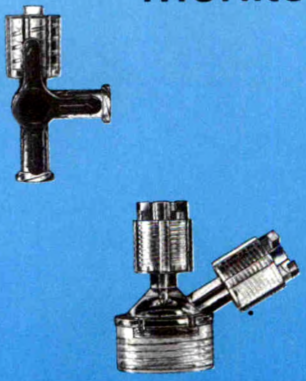

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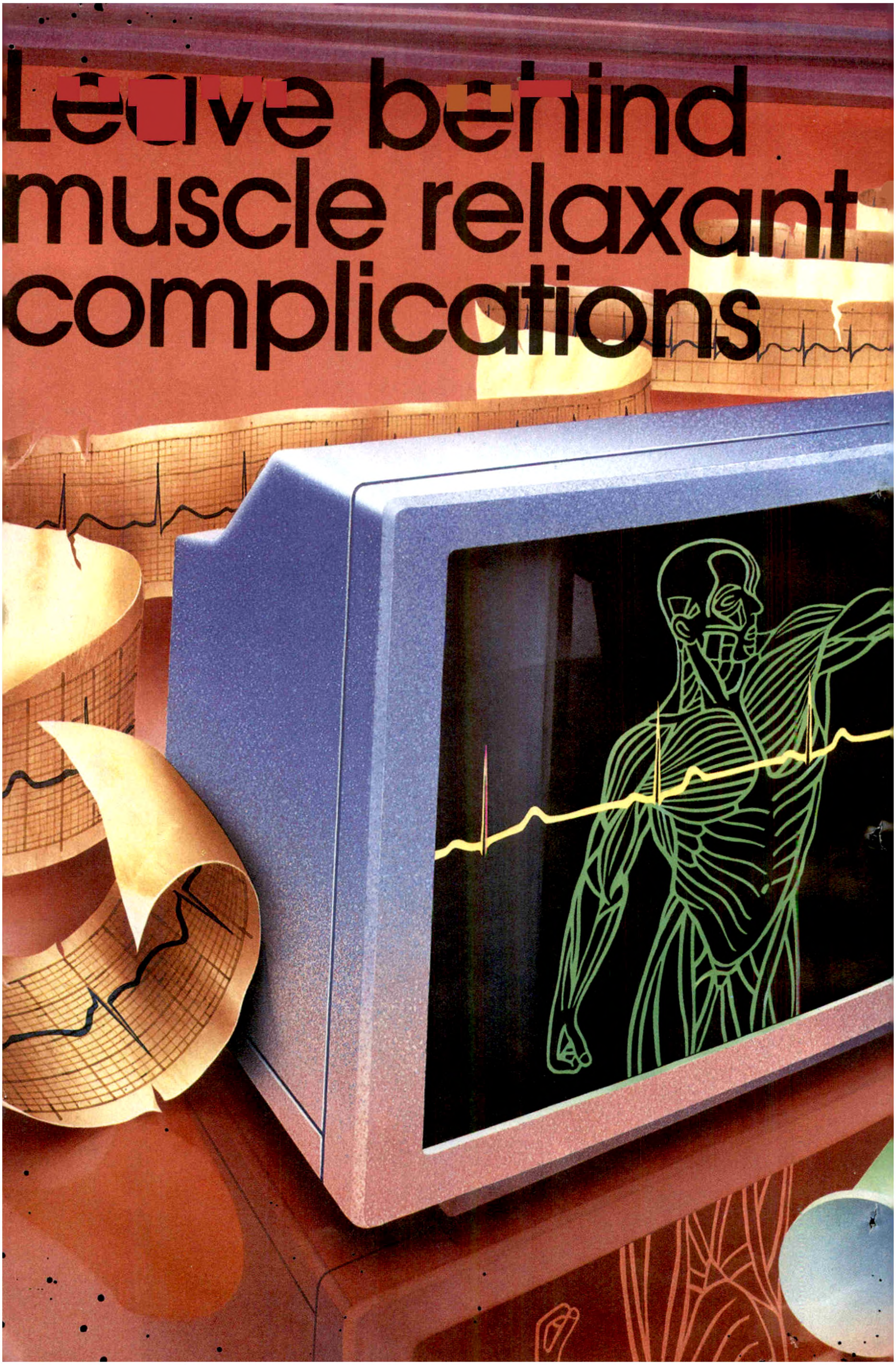
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1. Feldman SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 199-200
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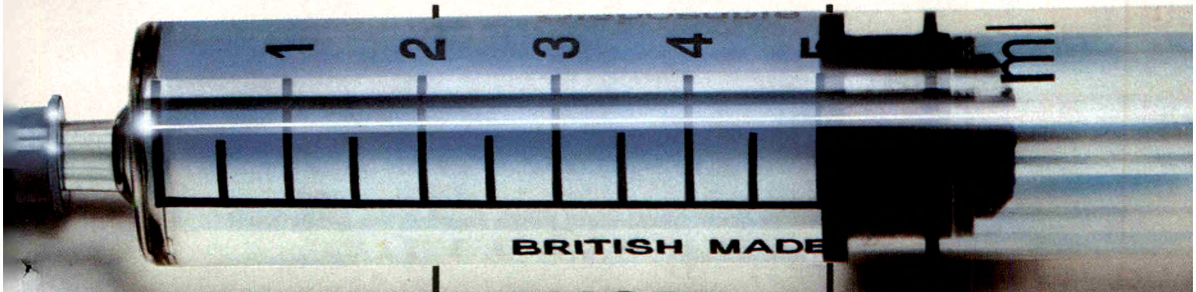

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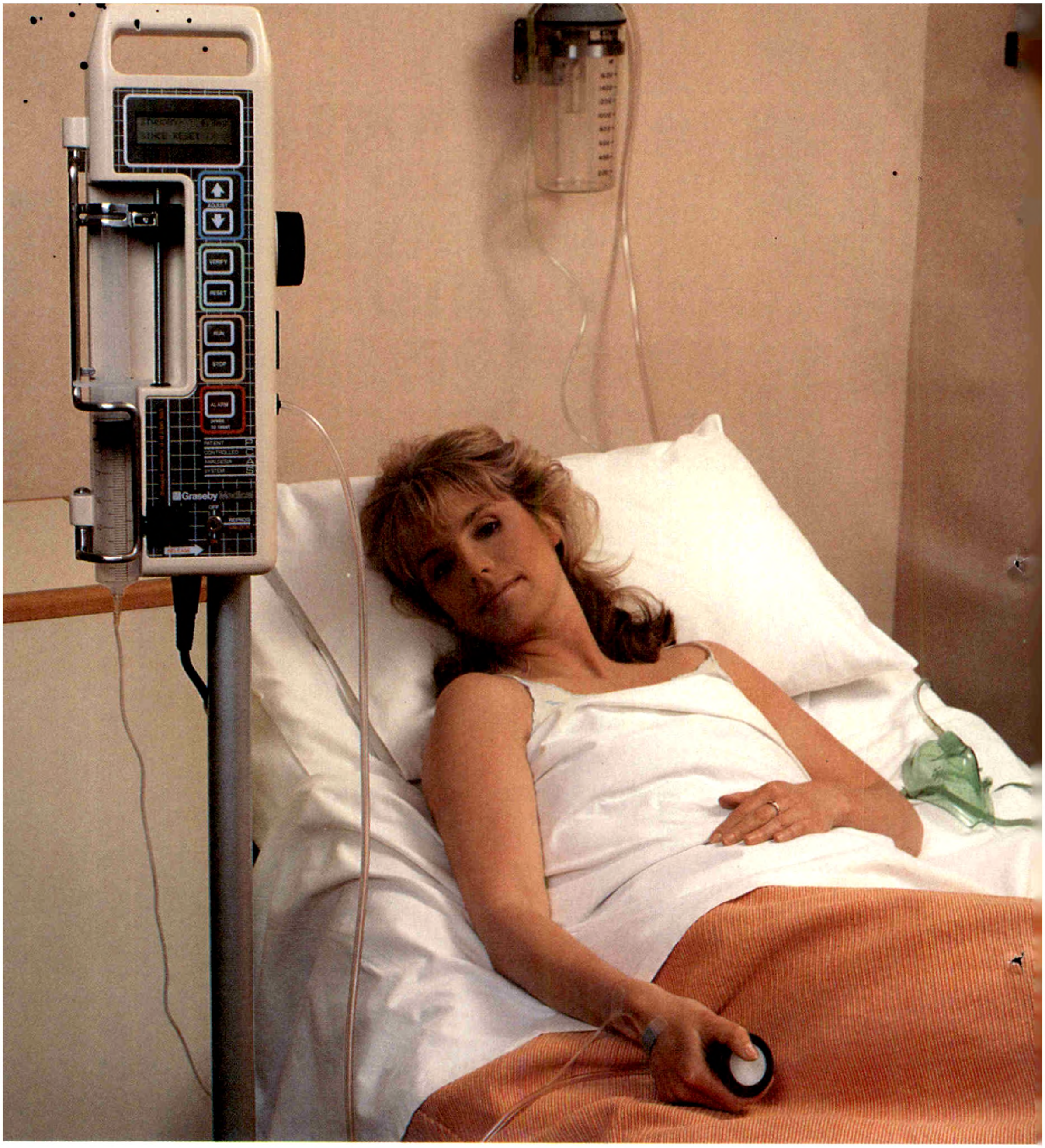

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Editorial

The confidential enquiry into maternal deaths

The recently published Report on Confidential Enquires into Maternal Deaths 1979–1981[1] represents the 10th in a series that has now covered 30 years. The mechanism of the enquiry remains the same as in previous years, but some changes have been made in its presentation. The term *avoidable factor* has been abandoned since it was sometimes interpreted as meaning that avoiding these factors would have prevented the death. It has been replaced by *substandard care*, which encompasses not only failures of clinical care, but also any other factors leading to a low standard of care, such as shortage of resources for staffing, administrative failures and inadequate back-up facilities. The form MCW 97, which is used to collect information on maternal deaths, has now been modified so as to encourage reporting of such factors and has been in use since January, 1985. Another change is the inclusion of a section on *late* deaths. The International Classification of Deaths defines a maternal death as occurring within 42 days of the termination of pregnancy, however long its duration, but this new section, in which there were 66 deaths, (none associated with anaesthesia) includes those who died between 43 days and 1 year after delivery.

In the 3-year period 1979–1981, there were 22 deaths directly attributable to anaesthesia, and a further seven in which administration of an anaesthetic made a contribution. All 22 deaths were associated with substandard care. The number represents an improvement on the previous three reports, when 37, 30 and 28 respectively, died as a direct result of an anaesthetic. The operative procedure most commonly involved was emergency Caesarean section.

Many deaths have more than one cause, but an attempt has again been made to classify them. Inhalation of gastric contents was the commonest cause; this occurred in eight patients and was precipitated by difficulty in intubation in three. Cricoid pressure[2] had been applied before tracheal intubation in six of these, but not at all in two. Application of cricoid pressure is an extremely effective method of preventing regurgitated material from entering the pharynx, so why did it fail? Was it applied too late? The force required for effective cricoid pressure is considerable,[3] and application prior to induction might cause distress to some patients. But was it applied properly? Enquiries of candidates in recent examinations have indicated that the majority do not apply cricoid pressure in the manner described by Sellick[2] and which he showed to be effective. Or was it released because of difficulty in introducing the laryngoscope? Perhaps, in the haste to achieve a rapid intubation, attempts at laryngoscopy were made too soon, before suxamethonium had taken full effect, and this, associated with a minimal and possibly too small a dose of the induction agent, might have provoked vomiting.

Five of these patients died of aspiration pneumonitis, and all had received magnesium trisilicate mixture during labour and before operation. Death cannot be attributed to acid aspiration in these patients, because the pH of the inhaled material was not measured, but in view of the therapy it is reasonable to assume that it would have been above the so-called critical value. Dissatisfaction with magnesium trislicate has been expressed for some time now and use of nonparticulate antacids has been advocated. However, in view of the very small number of deaths involved, it will be many years before, or indeed if, the question of which is the best antacid is answered. It is interesting to note, however, that even now magnesium trisilicate remains the most commonly used antacid in this country.[4]

Eight deaths were directly related to difficulty in tracheal intubation. In four patients, the tracheal tube was definitely in the oesophagus and four deaths were due to persistent attempts at intubation. There are a number of reasons why the obstetric patient is more difficult to intubate: they usually have full dentition, the thorax has been lifted into an unusual position by a wedge, there may be some degree of laryngeal oedema, incorrect application of cricoid pressure may distort and displace the larynx, the

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presence of large breasts and a hand applying cricoid pressure may make introduction of the laryngoscope difficult. The incidence of failure to intubate obstetric patients is not known, but a recent report[5] quoted a figure of 1 in 300. A comparison of maternal mortality figures with the report of Lunn and Mushin,[6] where there were four problems with tracheal intubation out of 58 deaths, tends to support the greater difficulty in obstetric patients. The figure of 1 in 300 might seem unduly high, but this could well be due to the fact that the use of a failed intubation drill is advocated early in the course of a difficult intubation.[7] What is obvious is that all anaesthetists and staff in labour wards must be familiar with a failed intubation drill and all necessary equipment to cope with a difficult intubation must be immediately at hand. Practising difficult tracheal intubation in the manner suggested by Cormack and Lehane[8] has much to recommend it.

As Scott[9] has pointed out, patients do not die from failure to intubate; they die from failure to stop trying to intubate or from undiagnosed oesophageal intubation. The only absolute diagnostic test of the latter is the absence of carbon dioxide in the exhaled gas, and this would require the presence of a capnograph on all units. A high level of suspicion of oesophageal intubation must always be borne in mind, and it is pertinent to remember that pre-oxygenation will delay the onset of cyanosis, possibly until after delivery of the baby. Gray[10] has recently commented on serious anaesthetic errors, and concluded with six very simple maxims, the first of which is 'When in doubt, take it out'. All anaesthetists must be competent at artificial ventilation using a mask, airway and bag.[9]

The other causes of death were again not new to these reports. Seven were due to substandard postoperative care. The difficulty of recognising cyanosis in oversedated patients with dark skins is again emphasised, as is the short duration of action of a single dose of naloxone in reversing the effects of narcotic analgesics. Two deaths were associated with inadequate reversal of neuromuscular blockade, achieved with pancuronium 6 mg and 7 mg respectively. Caesarean section is a relatively rapid operation and pancuronium is long acting, so one must query its use when shorter acting drugs are available. Three patients had severe disabling respiratory disease due to kyphoscoliosis. Other causes included a disconnexion in a ventilator system and cuff herniation of a tracheal tube causing respiratory obstruction. Haemorrhage is mentioned in the anaesthetic section, and although this is not an anaesthetic cause of death, the anaesthetist is in a unique position to assess and treat blood loss, and hence must take this responsibility. Unlike previous reports, epidural anaesthesia has not been implicated as a direct cause of death, but it is far too early yet to comment on whether the increasing use of the technique for Caesarean section is influencing mortality.

A factor which is repeatedly noted, is the frequency with which inexperienced anaesthetists are involved with these disasters. This subject has been discussed on many occasions and the answer is obvious. Another factor is the failure of obstetricians to consult with anaesthetists about difficult cases before urgent intervention is required, thus avoiding the involvement of an inexperienced person. Obstetricians must take full responsibility in such circumstances.

From 1952 to 1981, maternal mortality has fallen from 98.9 to 8.9 per 100 000 total births, that is by over 90 percent. Anaesthetists have always been in the front of medical audit, and in the preface are congratulated by the Chief Medical Officer for their efforts in this field. There are several ways of looking at anaesthetic related maternal mortality. Thus, there are 9.0 anaesthetic related deaths per million maternities, or, 12.6 percent of direct maternal deaths, a figure that has increased from 10.9 percent in 1970–1972, or, it is the third commonest cause of maternal death after hypertensive heart disease and pulmonary embolism.

The number of anaesthetic deaths in relation to the number of anaesthetics given is, however, much more important. No figures are available for the latter, although it may easily be deduced that there has been a marked increase in the last 10–15 years. Epidural analgesia as a form of pain relief in labour has only really been popular since 1968. The number of Caesarean sections has increased from 5.2 percent of maternities in 1970–1972 to 8.4 percent in 1979–1981; that is, from 103 310 to 157 850. In addition, from 1968–1981 there have been more than 1.4 million legal abortions. When viewed in this way, there has been an enormous *reduction* in anaesthetic related maternal mortality, of which obstetric anaesthetists, and the pioneers in the field in particular, can be justly proud. It is the production of these reports which has engendered such interest, but it is essential that anaesthetists maintain the standards of care and attention that have resulted in such a reduction in mortality and that they continue to fight for facilities so that further reductions can be achieved. Perhaps it is too much to expect, but one can only live in hope of reading 'There were no deaths in this triennium related to anaesthesia'.

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Triazolam premedication

A comparison with lorazepam and placebo in gynaecological patients

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Summary

A randomised, double blind study, of 58 female patients undergoing laparoscopic investigation was carried out to compare triazolam 0.25 mg, lorazepam 2 mg, or placebo as oral premedication. Each patient was assessed by only one of the authors both pre- and postoperatively with regard to anxiolysis, sedation and rapidity of recovery. Triazolam and lorazepam were each associated with a significant reduction in anxiety compared to the initial assessment, whereas placebo had no anxiolytic effect. Sixty minutes after premedication, patients who had received triazolam were significantly more sleepy than patients given placebo or lorazepam. Two hours after the operation, the patients who had had triazolam or lorazepam were significantly more sleepy than those who received placebo. However, at 6 hours postoperatively there was no difference between triazolam and placebo, whilst those who had been given lorazepam were still significantly more sleepy than those given placebo. Triazolam appears to offer advantages over either lorazepam or placebo in patients who require rapid recovery, sedation and reduction in pre-operative anxiety.

Key words

Premedication; lorazepam, triazolam.
Recovery; recall.

Day case surgery has become more popular for patients who are to undergo short, relatively minor, surgical procedures. If premedication is given to these patients, a conflict may result between the particular need for pre-operative sedation and anxiolysis, and the rapid recovery and clearheadedness required for discharge on the same day.

Triazolam is a triazolo-benzodiazepine which had previously been reported to be principally used for night sedation.[1,2] Its properties of rapid onset, short duration of action and short plasma half-life of 2.25 hours suggest it has potential value as premedication in day stay surgical patients. The aim of this study was to compare the adequacy of anxiolysis, sedation and rate of recovery of patients premedicated with triazolam, lorazepam or placebo.

Methods

Sixty female patients, assessed to be ASA 1, who were to undergo simple laparoscopic procedures, were randomly allocated to three groups of 20

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patients. Patients excluded from the trial were those who had pre-operative pain, were pregnant, over 60 years or under 16 years of age, patients who were either receiving benzodiazepines or gave a history of adverse reactions to benzodiazepines, patients on steroids, or drugs affecting the central nervous system or the cardiovascular system and patients who abused drugs or alcohol. The trial was approved by the Central Oxford research ethics committee and informed consent was obtained in writing from each patient. At the time of this study, all such patients remained in hospital overnight after the operation.

During the pre-operative visit, the investigating anaesthetist made a baseline assessment of the psychomotor state and recorded the systemic blood pressure, heart and respiratory rates. Weight and height were documented. Each patient was allocated in a double-blind, randomised manner to receive premedication with identical capsules of lorazepam 2 mg, triazolam 0.25 mg or placebo. The date of birth was recorded during the hospital admission procedure.

Sedation and anxiolysis were assessed using a self-rating multiple affect adjective check (MAAC) list[3,4] (see Appendix), a visual analogue test[5] and a psychomotor test.[6-8] The visual analogue test consisted of three 10-cm lines representing opposite extremes of the patient's state, namely calm to anxious, alert to asleep, clearheaded to dizzy. Analysis of visual analogue scales was based on the distance the mark was placed on the line from the left hand end of the scale. Thus, higher scores indicated increased anxiety, sleepiness or dizziness. The results were analysed separately in patient and physician groups by analysis of variance (ANOVA).

The anaesthetist was separately required to complete a visual analogue test identical to the one completed by the patient as another measurement of the patient's sedation and anxiolysis. The psychomotor test consisted of a sheet of paper with lines of lower and upper case letters and numerals. The patient was asked to circle only the lower case letters starting in the top left hand corner, and moving as swiftly as possible from left to right, line by line, down the page over a timed 2-minute period. These tests were carried out at initial assessment, 60 minutes after premedication and in the anaesthetic room prior to induction of anaesthesia.

Immediately prior to induction of anaesthesia, the patient was briefly shown a £5 note and recall of this was tested during early recovery from the anaesthetic. All patients received a standard anaesthetic induction: pretreatment with tubocurarine 3 mg followed by thiopentone 5 mg/kg. Relaxation for tracheal intubation was obtained with 1.3 mg/kg suxamethonium and 1 μg/kg of fentanyl was also given at this stage. Intermittent positive pressure ventilation of the lungs was continued with a ventilator (Nuffield 200, Penlon) adjusted to deliver approximately 100 ml/kg/minute of fresh gas flow through a Bain system. Anaesthesia was maintained with nitrous oxide 70%, oxygen and halothane initially at 2 percent inspired concentration, with a rapid reduction to 0.5 percent.

The duration of anaesthesia from induction to the end of surgery was noted. Recovery was assessed at 1-minute intervals in the recovery room by a trained nurse, who noted the time taken from the end of surgery to the time the patient first opened her eyes to command, repeated at 1-minute intervals, and noted also when the patient was able to state her date of birth correctly in response to the request, also repeated at 1-minute intervals. The psychomotor tests, together with the other tests of anxiety and sedation, were all repeated at 30 minutes, and at 2, 4, and 6 hours after termination of anaesthesia. All assessments of any one patient were made by only one of the authors, who also administered the anaesthetic. Only mild, oral analgesics (Distalgesic (Dista) or paracetamol) were given postoperatively.

Results

Twenty patients received triazolam, 19 received lorazepam and 19 the placebo. Two other patients were excluded after a change in surgical plan. There were no significant differences by analysis of variance between the patients in each drug group in age, weight or height (Table 1); nor were there significant differences at any time in systemic blood pressure, pulse or respiration between groups.

No differences were apparent by analysis of variance between groups when the following were compared: duration of anaesthesia, time until patient first opened her eyes, time until the patient first correctly stated her date of birth and the ability to recall the test of memory accurately.

Table 1. Demographic data, mean (SD)

Group	Triazolam	Lorazepam	Placebo
Age, years	32.1 (6.1)	32.6 (7.5)	32.1 (6.7)
Weight, kg	61.1 (13.2)	61.7 (12.7)	61.8 (9.3)
Height, metres	1.63 (0.07)	1.62 (0.05)	1.60 (0.08)
Number	20	19	19

There were no significant differences between drug groups by analysis of variance.

Table 2. Physician's ratings; visual analogue scales, mean value (SD). Baseline values and times to assessment postoperatively

Calm–anxious	Triazolam	Lorazepam	Placebo
baseline	37(24)	49(27)	48(25)
Change at 60 minutes	−23(23)†	−28(21)‡	−20(22)*
at induction	−17(26)*	−23(26)†	−11(33)
Alert–asleep			
baseline	8(8)	8(7)	7(5)
Change at induction	+28(31)‡	+15(18)†	+12(21)*
at +2 hours	+46(22)‡	+55(26)‡	+29(29)‡
at +4 hours	+17(22)†	+29(27)‡	+23(28)†
at +6 hours	+2(15)	+17(24)*	+4(11)
Clearheaded–dizzy			
baseline	6(4)	10(11)	7.5(5)
Change at induction	+22(25)‡	+11(15)†	+13(21)*
at +2 hours	+39(18)‡	+37(21)‡	+23(25)‡
at +4 hours	+13(12)‡	+19(23)†	+12(18)*
at +6 hours	+4(13)	+5(17)	+6(16)

The baseline values are the initial distance in mm from the left hand of the visual analogue scale to where the patient placed a mark. The subsequent values are the mean change from the initial mean value.

Key: Comparisons within drug group between time points (analysis of variance) *$p < 0.05$; †$p < 0.01$; ‡$p < 0.001$.

Physician's assessments

Assessment of calmness. There was no significant difference between drug groups (Table 2). At the time of induction of anaesthesia, patients who had received triazolam or lorazepam, were significantly less anxious compared to their baseline assessment, whereas there was no effect in patients given the placebo.

Increased sleepiness. This occurred in all patients 60 minutes after premedication, even in those given placebo. There was no signficant difference until 2 hours postoperatively, when patients given lorazepam were significantly ($p < 0.01$) more sleepy than those given placebo. At 6 hours postoperatively, patients who had received lorazepam were significantly ($p < 0.05$) more sleepy than those who had either triazolam or placebo, who were as alert as at baseline.

Assessment of clearheadedness. All the patients were significantly more dizzy by the time of induction compared to baseline. Two hours after anaesthesia, patients in the triazolam group were significantly less clearheaded than the placebo group, but all patients appeared to be as clearheaded 6 hours after anaesthesia as at baseline.

Patient's assessments

Assessment of anxiety. Prior to premedication, assessment of anxiety showed an imbalance between the treatment groups; the triazolam group was significantly more calm than the placebo group ($p < 0.005$) (Table 3). Patients who received triazolam remained more calm throughout the investigation than the placebo group. At 60 minutes, a significant reduction in anxiety relative to baseline was seen in the lorazepam group, but not at induction, whereas the placebo group were more calm at induction than at baseline.

Increased sleepiness. Sixty minutes after premedication, patients given triazolam were more sleepy than those given placebo ($p < 0.05$). Two hours postoperatively, both triazolam and lorazepam groups were significantly ($p < 0.01$ for

Table 3. Patient's ratings; visual analogue scales, mean value (SD). Baseline values and times to assessment postoperatively

Calm–anxious	Triazolam	Lorazepam	Placebo
baseline	28(27)	36(26)	45(22)
Change at + 60 mins.	−7(41)	−14(15)†	−18(31)
at induction	+0.5(38)	−8(37)	−9(19)*
Alert–asleep			
baseline	16(23)	19(20)	14(23)
Change at 60 mins.	+43(32)‡	+27(24)‡	+18(28)
at + 2 hours	+58(24)‡	+55(30)‡	+32(33)‡
at + 6 hours	+12(37)	+30(38)†	+7(21)
Clearheaded–dizzy			
baseline	6(6)	14(15)	9(12)
Change at 60 mins	+40(31)‡	+18(17)†	+14(27)
at + 2 hours	+51(29)‡	+42(44)‡	+27(26)‡

Key: (as for Table 2) *$p<0.05$; †$p<0.01$; ‡$p<0.001$.

triazolam and $p<0.05$ for lorazepam) more sleepy than the placebo group. However, at 6 hours postoperatively, there was no difference between triazolam and placebo patients, who had both returned to baseline values, whereas the lorazepam group were still significantly ($p<0.05$) more sleepy than the placebo group.

Assessment of clearheadedness. At baseline, again, there was an imbalance, since the triazolam patients were significantly more clearheaded than the lorazepam patients ($p<0.05$). At 60 minutes after premedication, the patients given triazolam were significantly less clearheaded than those in either the placebo ($p<0.05$) or the lorazepam ($p<0.05$) groups. At 2 hours postoperatively, the triazolam patients were significantly less clearheaded than those given placebo ($p<0.05$), but not different to those given lorazepam. At the 4- and 6-hour intervals postoperatively, there were no significant differences between groups; however, all patients rated themselves less clearheaded than at baseline.

Psychomotor test score. This was analysed by the median test. The median value of the pooled data was found, and each patient's results were then compared to the median. At 2 hours postoperatively, the lorazepam group differed by having significantly ($p=0.003$) more patients who achieved scores below the median value (15 of 18) than the placebo (6 of 18) and triazolam groups (6 of 17).

Multiple affect adjective check (MAAC) list (see Appendix). At baseline, there was a difference between triazolam and placebo groups which was close to significance at the 5 percent level (Kolmogorov-Smirnov test). Thus, the triazolam group appeared to be less anxious.

The Kolmogorov-Smirnov test was also used to test the significance of the difference in MAAC score from baseline between drug groups. At 2 hours postoperatively, the difference between MAAC scores of the triazolam and placebo groups was significant ($p<0.05$), and the triazolam group showed less reduction from the initial score. However, this group had started in the study in a less anxious state. There were no significant differences between any of the three groups at 4 or 6 hours postoperatively.

Discussion

The purpose of this study was to evaluate the effectiveness and recovery from triazolam premedication for patients undergoing minor surgery. Assessment of the value of premedication is difficult, since the requirements will vary from patient to patient, and between anaesthetists. Although reduction of anxiety is the prime requirement of premedication,[9,10] the anaesthetist may welcome increased sedation to facilitate anaesthesia. The ideal premedicant should relieve anxiety, and any sedative or unpleasant side effects should be minimal and short-lasting to allow rapid recovery. The only other report of the use of triazolam for premedication failed to distinguish between the property of anxiolysis and the side effect of hypnosis.[11]

It is difficult to achieve rapid reduction in anxiety by pharmacological means in the short interval between admission for day surgery and the time the patient reaches the operating theatre. The use of sufficiently high doses of sedative drugs to achieve rapid anxiolysis may also prolong recovery. Nonpharmacological means of reducing anxiety, such as a pre-operative visit by the anaesthetist, are well known also to reduce anxiety,[12,13] but the circumstances of rapid turnover of patients in day surgery units makes it difficult to achieve the maximum benefit by such a time-consuming task.

Triazolam has been extensively used to produce night sedation,[1,2] particularly in the elderly,[1] and has also been used specifically for night sedation in pre-operative patients,[14,15] where its properties of rapid onset and lack of residual effects[1] have proved useful. Lorazepam has become commonly used for premedication largely because, unlike diazepam, it has a shorter duration of action—partly due to lack of active metabolites[16] and because it does not undergo enterohepatic recirculation. Nonetheless, its duration of action is longer than ideal for day case patients and prolonged amnesia is particularly undesirable in ambulant patients.

The use of complex tests of psychological state, recall and subjective feelings is open to criticism if the patients are unfamiliar with the terms used. This series of patients is unusual in consisting of young, healthy females who were highly motivated, and well acquainted with hospital procedures and personnel. Our findings may not, therefore, be applicable to the population in general. The applicability of the tests used in this study for complicated actions as driving a motor car or tasks requiring higher cerebral activity is limited, but more complex tests were beyond the scope of this study.

The need for pharmacological premedication is demonstrated in this study by the anaesthetists who found a reduction in pre-operative anxiety in premedicated patients compared to those who received placebo. This difference occurred despite the involvement of an anaesthetist in assessing each patient, gaining voluntary consent and visiting the patient at least four times before induction of anaesthesia. The requirement of alertness for discharge at 6 hours postoperatively was met by all unpremedicated patients and all who had received triazolam, whereas patients who had received lorazepam were still less alert than before premedication. The tests of psychomotor skills similarly demonstrated that only those patients who had had lorazepam failed to recover completely by 4 hours. This test may be influenced by learning, and although enhanced performance was found in some patients in all groups pre-operatively, the numbers who did so are insignificant.

Our results are in marked contrast to those of Pinnock *et al.*[11] whose patients found triazolam to be a sedative hypnotic, devoid of anxiolytic effect, but in whom the anaesthetist's assessments did not attempt to distinguish between calmness and hypnosis, and failed also to distinguish between the effects of placebo, triazolam, or diazepam in alertness at 6 hours.

In conclusion, oral triazolam 0.25 mg produces effective pre-operative anxiolysis and sedation. Recovery from these desired effects, and associated other effects, occurs within 6 hours of surgery. Triazolam appears to have a place as a premedicant for short stay surgical patients.

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Appendix. Multiple affect adjective test list[3]

Patient ticks the words which describe how she feels at that moment.

afraid
desperate
fearful
frightened
nervous
panicky
shaky
tense
terrified
upset
worrying

calm
cheerful
contented
happy
joyful
loving
pleasant
secure
steady
thoughtful

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Arterial to end tidal carbon dioxide tension difference during Caesarean section anaesthesia

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Summary

The relationship between arterial carbon dioxide tension and end tidal carbon dioxide tension was studied in 19 patients during general anaesthesia for Caesarean section. Thirteen patients scheduled for elective abdominal hysterectomy formed a nonpregnant group. There was significant correlation between arterial and end tidal CO_2 tensions in both groups. During Caesarean section, this difference was significantly less than in the nonpregnant group.

Key words

Anaesthesia, obstetric; Caesarean section.
Measurement techniques; capnography.

Measurement of end tidal carbon dioxide tension ($P\text{E}'\text{CO}_2$) is a noninvasive procedure commonly used to monitor ventilation. The difference between end tidal and arterial carbon dioxide tension ($P\text{aCO}_2$) in healthy adults under general anaesthesia has been evaluated by Nunn *et al.*[1] (0.63 kPa, SD 0.33, range 0.22–1.21 kPa), Ramwell,[2] Fletcher and Jonson[3] (median 0.6 kPa at small tidal volumes and 0.3 kPa at large tidal volumes) Takki *et al.*[4] (0.46 kPa, SEM 0.26 kPa), Askrog *et al.*[5] (0.66 kPa, SEM 0.36) and Raemer *et al.*[6] (mean 0.54 kPa).

We were unable to find a study which evaluated the arterial to end tidal CO_2 difference during late pregnancy or Caesarean section. Kneeshaw *et al.*[7] in their study on assessment of fresh gas flows using a Bain system, assumed the $P\text{aCO}_2 - P\text{E}'\text{CO}_2$ in late pregnancy to be the same as that in nonpregnant subjects. Because there are many physiological changes in ventilation and perfusion during pregnancy,[8–10] we planned this study to evaluate the difference between $P\text{aCO}_2$ and $P\text{E}'\text{CO}_2$ and to determine the difference between pregnant and nonpregnant females.

Methods

The protocol for the study was approved by the hospital ethical committee and informed written consent was obtained from all patients.

The nonpregnant group consisted of 13 female patients scheduled for abdominal hysterectomy who had no cardiac or respiratory abnormalities and had never smoked(ASA 1). They were premedicated with pethidine 1.5 mg/kg, promethazine 0.5 mg/kg, and atropine 0.6 mg intramuscularly one hour prior to induction of anaesthesia which was achieved with 3–5 mg/kg of thiopentone. Tracheal intubation with a cuffed tube followed the administration of 1–1.5 mg/kg suxamethonium. Anaesthesia was maintained with a mixture of 33% oxygen in nitrous oxide, 0.5

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to 1% halothane and relaxation with pancuronium. Ventilation was controlled with a Siemens 900 B ventilator, with tidal volume of 10 ml/kg and respiratory frequency of 14 breaths/minute. Twenty-five minutes after induction of anaesthesia, arterial blood was sampled from the left radial artery for analysis and $P\mathrm{E'CO_2}$ determined at the same time.

The $P\mathrm{E'CO_2}$ was measured continuously using Siemens-Elema CO_2 analyser 930 at the proximal end of the tracheal tube. The analyser was calibrated at regular intervals with a known concentration of CO_2. The $P\mathrm{aCO_2}$ was measured using a Corning blood gas analyser (165/2), after two-point calibration before each sample, at 37°C. Blood gas analysis was performed immediately after obtaining the samples.

The pregnant group comprised 19 patients undergoing elective or emergency Caesarean section under general anaesthesia. None of the patients was suffering from pre-existing cardiovascular or respiratory disease and only nonsmokers were admitted to the study. All patients received 30 ml of magnesium trisilicate before induction and anaesthesia was induced with the patients in a 15° left lateral tilt.

After pre-oxygenation for 5 minutes, anaesthesia was induced with 3–5 mg/kg of thiopentone followed by suxamethonium 1.5 mg/kg and the trachea was intubated with a cuffed tube while cricoid pressure was applied. Anaesthesia was maintained with a mixture of 50% oxygen in nitrous oxide with 0.5% halothane and pancuronium 0.05 mg/kg used to maintain relaxation. After delivery of the baby, anaesthesia was maintained with 33% oxygen in nitrous oxide with opioid supplements. Ventilation was controlled with a Siemens 900 B ventilator with a tidal volume of 10 ml/kg and a respiratory frequency of 14 breaths/minute. Arterial blood was drawn from the left radial artery just before uterine incision and a second sample drawn at 25 minutes following induction and analysed immediately. The $P\mathrm{E'CO_2}$ was determined at both instances.

Nasopharyngeal temperatures were monitored in all patients and blood gases were corrected to the body temperature.[11] Nitrous oxide corrections were made to all the end tidal CO_2 measurements of the CO_2 analyser.[12]

The paired *t*-test was used to evaluate the statistical significance between the variables within the groups and the unpaired *t*-test was used in between groups. Regression analysis was performed between $P\mathrm{aCO_2}$ and $P\mathrm{E'CO_2}$ with the $P\mathrm{aCO_2}$ formula as independent variable (x) in both groups and the parameters of the regression equation and confidence limits were calculated.

Results

Table 1 shows the mean ages, $P\mathrm{aCO_2}$, $P\mathrm{E'CO_2}$ (a − E') $P\mathrm{CO_2}$ and p values for the nonpregnant group. Table 2 shows the same data for the pregnant group.

In the pregnant group, the $P\mathrm{aCO_2}$ was very close to the $P\mathrm{E'CO_2}$. The (a − E') $P\mathrm{CO_2}$ was 0.004 (SEM 0.082) kPa at predelivery sampling and 0.104 (SEM 0.087) at 25 minutes. The difference between the arterial end tidal CO_2 differences for the nonpregnant and pregnant groups (both at predelivery and at 25 minutes) were significant. However, there was no significant difference between (a − E') $P\mathrm{CO_2}$ at predelivery and at 25 minutes within the pregnant group.

There was a positive correlation between $P\mathrm{aCO_2}$ and $P\mathrm{E'CO_2}$ in both groups. The regression analysis of $P\mathrm{aCO_2}$ (x) and $P\mathrm{E'CO_2}$ (y) for all the groups with their confidence intervals are shown in Table 3 and Fig. 1. The confidence intervals of the nonpregnant group were larger than the pregnant group, probably because of the narrow range of $P\mathrm{aCO_2}$ (x).

Table 1. Nonpregnant group

		At 25 minutes		
	Age (years)	$P\mathrm{aCO_2}$ kPa	$P\mathrm{E'CO_2}$ kPa	(a − E') $P\mathrm{CO_2}$ kPa
	27	3.53	2.58	0.95
	23	3.16	2.29	0.87
	26	2.88	2.11	0.77
	21	3.21	2.54	0.67
	28	3.33	2.60	0.73
	31	3.14	2.68	0.46
	27	3.34	2.61	0.73
	29	3.52	2.89	0.63
	29	3.28	2.46	0.82
	33	3.53	2.96	0.57
	21	3.16	2.64	0.52
	21	3.60	2.85	0.75
	22	3.21	2.54	0.67
Mean	26	3.299	2.596	0.703
SEM	1.13	0.05	0.06	0.0382
p				< 0.001

Table 2. Pregnant group

	Age (years)	Predelivery			At 25 minutes		
		Pa_{CO_2} kPa	$P_{E'}CO_2$ kPa	(a − E′) kPa	Pa_{CO_2} kPa	$P_{E'}CO_2$ kPa	(a − E′) kPa
	25	4.47	4.56	−0.09	4.33	3.74	0.59
	27	3.57	3.67	−0.1	3.17	3.06	0.11
	24	4.42	3.83	0.59	3.09	3.01	0.08
	20	4.23	3.64	0.59	3.36	2.94	0.42
	21	3.56	3.42	0.14	3.78	2.88	0.9
	22	3.04	3.67	−0.63	2.90	3.43	−0.53
	22	3.53	3.71	−0.18	3.20	3.29	−0.09
	23	3.52	3.69	−0.17	3.2	3.27	−0.07
	25	3.77	4.12	−0.35	3.21	3.36	−0.15
	21	4.49	4.24	0.25	3.80	4.05	−0.25
	22	3.97	4.15	−0.18	3.65	3.97	−0.32
	25	4.32	4.10	0.22	3.04	3.36	−0.32
	24	3.77	3.37	0.4	3.45	3.23	0.22
	25	3.53	3.49	0.04	3.24	3.24	0
	28	2.70	3.28	−0.58	2.52	2.55	−0.03
	24	3.77	3.88	−0.11	3.08	3.01	0.07
	25	2.86	3.26	−0.4	3.14	3.07	0.07
	25	4.33	3.97	0.36	3.48	2.71	0.77
	23	4.13	3.85	0.28	3.33	2.82	0.51
Mean	23.7	3.788	3.784	0.004	3.314	3.210	0.104
SEM	0.48	0.12	0.08	0.082	0.08	0.09	0.087
p				n.s.			n.s.

n.s., not significant.

Table 3. Regression analysis of Pa_{CO_2} (x), $P_{E'}CO_2$ (y)

Group	n	Correlation (r)	Regression equation	Confidence interval of b (at $p = 0.05$)
Nonpregnant	13	0.807*	$y = 0.915x - 0.42$	0.291–1.539
Pregnant				
predelivery	19	0.748*	$y = 1.94 + 0.485x$	0.389–0.583
postdelivery	19	0.522†	$y = 1.45 + 0.531x$	0.262–0.800

*$p < 0.001$.
†$p < 0.05$.

Discussion

In our study, (a − E′) P_{CO_2} in nonpregnant patients undergoing abdominal hysterectomy was found to be 0.703 (SEM 0.0382) kPa (range 0.46–0.95 kPa). This is comparable to that reported by Nunn *et al.*[1] 0.63 (SD 0.33) (range 0.22–1.21 kPa) and Askrog *et al.*[5] (0.66 SEM 0.36 kPa).

In the pregnant group, however, the Pa_{CO_2} was very close to $P_{E'}CO_2$ predelivery and after 25 minutes (the difference between Pa_{CO_2} and $P_{E'}CO_2$ was not statistically significant). The observed difference between the two groups is probably due to the many physiological changes that occur in late pregnancy such as increased minute ventilation, increased cardiac output, haemodilution and increased blood volume.[8–10] These result in increased perfusion of the alveoli and better gaseous exchange. The (a − E′) P_{CO_2} was negative in 50% of instances in the pregnant group.

Fletcher *et al.* reported negative or zero (a − E′) P_{CO_2} in 12% of patients. They postulated that large tidal volumes and a low frequency of ventilation leads to a positive slope of Phase III of the SBT − CO_2 tracing (single breath test for carbon dioxide which is a tracing

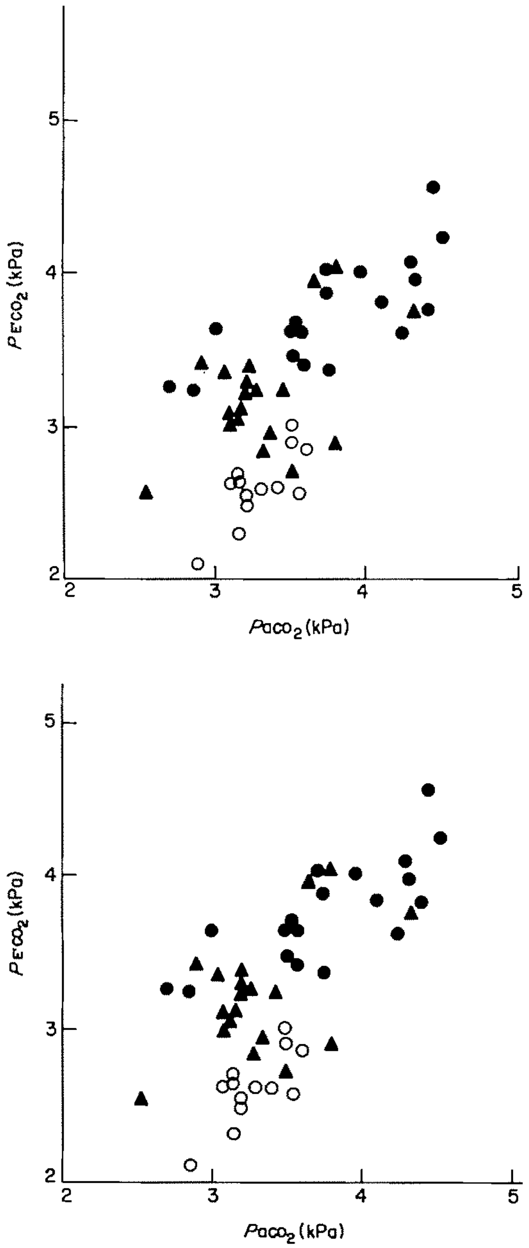

Fig. 1. $P\mathrm{aCO}_2$ (x) versus $P\mathrm{E'CO}_2$ (y). ○, Nonpregnant group ($r = 0.807$, $p < 0.001$); ●, predelivery in pregnant group ($r = 0.748$, $p < 0.001$); ▲, 25 minutes after induction in pregnant group ($r = 0.522$, $p < 0.05$).

of expired $P\mathrm{CO}_2$ against tidal volume).[3] Therefore $P\mathrm{E'CO}_2$ exceeds temporal mean alveolar carbon dioxide tension.[3,13] This temporal mismatching of ventilation and perfusion produces a ventilation–perfusion time-dependent alveolar deadspace. Temporal deadspace implies that $P\mathrm{aCO}_2$ varies during the respiratory cycle. Pregnancy is associated with a reduction of functional residual capacity[14] and increased carbon dioxide production compared to nonpregnant individuals. The $P\mathrm{aCO}_2$ fluctuations during the respiratory cycle would be greatest when functional residual capacity is small. This, along with increased CO_2 production per breath explains the greater incidence of occurrence of a positive Phase III slope during Caesarean section anaesthesia.[3,13]

Raemer *et al.*[6] have shown that several factors, namely changes in blood pressure, pulmonary blood flow, variations in compliance, anaesthetic agents and surgical position, lead to alteration in ventilation to perfusion ratio. This can produce changes in physiological dead space that are reflected by a varying (a − E′) $P\mathrm{CO}_2$. These factors are more likely to be associated with Caesarean section anaesthesia and would explain the wider degree of scatter observed between $P\mathrm{aCO}_2$ and $P\mathrm{E'CO}_2$ in the pregnant group[6,15–19] (Fig. 1 and Table 3).

By applying regression analysis, the $P\mathrm{E'CO}_2$ equivalent to $P\mathrm{aCO}_2$ of 4.2 kPa (which is the optimum $P\mathrm{aCO}_2$ at delivery of the baby during Caesarean section)[7] would be 3.97 kPa with a (a − E′) $P\mathrm{CO}_2$ of 0.22 kPa, whereas for a similar $P\mathrm{aCO}_2$, the equivalent $P\mathrm{E'CO}_2$ in nonpregnant patients would be 3.42 kPa with an (a − E′) $P\mathrm{CO}_2$ of 0.77 kPa.

This study has shown a significant difference between (a − E′) $P\mathrm{CO}_2$ between patients undergoing Caesarean section anaesthesia and nonpregnant subjects. The (a − E′) $P\mathrm{CO}_2$ is less during Caesarean section anaesthesia than in the nonpregnant patients undergoing abdominal hysterectomy. At a $P\mathrm{aCO}_2$ of 4.2 kPa the (a − E′) $P\mathrm{CO}_2$ would be 0.22 kPa at predelivery during Caesarean section.

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Nitrous oxide anaesthesia and vomiting

The effect of nitrous oxide anaesthesia on the incidence of vomiting following gynaecological laparoscopy

D. S. LONIE AND N. J. N. HARPER

Summary

Eighty-seven patients undergoing routine laparoscopy were divided randomly into two groups to study the effect of nitrous oxide anaesthesia on the incidence of postoperative vomiting. Patients in group A received nitrous oxide as part of their anaesthetic, while in group B nitrous oxide was omitted. Significantly fewer patients in group B vomited when compared with group A (17 percent and 49 percent respectively; $p < 0.005$). We suggest that an anaesthetic technique which avoids nitrous oxide may be especially indicated in patients undergoing laparoscopy.

Key words

Anaesthetics, gases; nitrous oxide.
Complications; vomiting.

Postoperative vomiting is an unpleasant and potentially dangerous event.[1] Its incidence is very variable,[2] depending, amongst other factors, on individual predisposition, age and sex;[1] the younger female patients are more likely to vomit. A high incidence of nausea and vomiting has been observed following gynaecological laparoscopy[3-5] and this has been attributed to the use of nitrous oxide as part of the anaesthetic technique.[6] Nitrous oxide may be implicated in postoperative vomiting due to its central and peripheral effects.[1,7] This study was designed to evaluate the incidence of nausea and vomiting in our practice and to investigate the effect of omitting nitrous oxide from the anaesthetic.

Patients and methods

Following local ethical committee approval, written informed consent was obtained from 93 patients (ASA 1 or 2) who were scheduled for elective inpatient laparoscopy on one consultant gynaecologist's routine morning list.

Patients were allocated randomly to one of two groups. All patients were premedicated with diazepam 10 mg orally one hour pre-operatively. They were pre-oxygenated for 3 minutes, using a transparent face mask, prior to induction of anaesthesia with thiopentone 4–6 mg/kg administered intravenously. Muscle relaxation was achieved with vecuronium bromide 0.1 mg/kg and the patient's trachea was intubated after 120 seconds. Manual inflation of the lungs was not performed prior to tracheal intubation. Anaesthesia was supplemented with fentanyl 2 μg/kg. In group A, anaesthesia was maintained with nitrous oxide 67 percent in oxygen and 1.25 percent minimum alveolar concentration (MAC) end tidal enflurane (0.7 percent) and in group B with 33 percent oxygen in nitrogen and 1.25

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MAC end tidal enflurane (2.1 percent). The enflurane concentration was measured with an infrared analyser (Datex Normac). End tidal carbon dioxide was measured with a capnograph (Gould Mk IV) and all patients were ventilated to normocapnia. The pulse rate, systolic arterial blood pressure and electrocardiograph were monitored. In most patients, neuromuscular blockade was monitored by stimulating the ulnar nerve using the train-of-four pattern of stimulation. Additional doses of vecuronium and fentanyl were given to patients in both groups when required.

For the surgical procedure, the patients were placed in a modified lithotomy position with a steep Trendelenburg tilt. The peritoneal cavity was inflated using a carbon dioxide pneumoflator (WISAP). The maximum intraperitoneal pressure measured was approximately 20 mmHg. At the end of the procedure, residual neuromuscular blockade was reversed with atropine 1.0 mg and neostigmine 2.5 mg administered intravenously. All patients received 100 percent oxygen and pharyngeal suction. Following extubation, patients were placed in the lateral position and patency of the airway maintained by supporting the jaw. The time of extubation and whether the patient retched or vomited were recorded. The patient was then transferred to the recovery room. All patients were prescribed papaveretum 10 mg intramuscularly for pain and prochlorperazine 12.5 mg intramuscularly for nausea as required.

In the recovery room the nurse in charge of the patient was asked to record any nausea or vomiting and the time of any postoperative medication. In the ward, the following morning, the patients were interviewed by a senior nurse who was unaware of which anaesthetic the patient had received. Patients were questioned about their emetic symptoms since regaining consciousness.

Statistical analysis of the results was performed using the Chi squared test with Yates' correction and the Mann Whitney U-test where appropriate. The null hypothesis was rejected when $p < 0.05$.

Results

There were 44 patients in group A and 49 patients in group B, with three exclusions in each group. Two patients in group A were difficult to intubate for anatomical reasons and required inflation with the facemask prior to intubation. The third exclusion in group A was due to inadequate documentation. In group B, one patient was excluded due to her sickle cell status, another patient proceeded to laparotomy and the third patient gave a history of allergy to thiopentone. The two groups were well matched for age, weight, duration of anaesthesia and dose of fentanyl as shown in Table 1.

Significantly fewer patients in group B vomited than in group A—17 percent compared with 49 percent ($p < 0.005$). The incidence of nausea was similar in the two groups—group A 49 percent and group B, 46 percent (Table 2). The difference between the two groups remained significant when the postoperative period was divided into early (in the recovery room, $p < 0.005$) and late (in the ward, $p < 0.05$ (Table 3). There was no difference between the groups with respect to postoperative medication requirements in the recovery room or on the ward ($p > 0.05$) (Table 4). When the patients requiring postoperative medication in recovery were excluded from the statistical analysis, the incidence of vomiting in the ward was still significantly different between the two groups ($p < 0.01$).

Neither postoperative vomiting after previous anaesthesia, nor a history of nausea when hungry had an effect on the incidence of vomiting. Only two patients in each group admitted to motion sickness.

The groups were well matched for duration of anaesthesia (Table 1), but there was a tendency within each group for patients undergoing the longer procedures to vomit, but the difference

Table 1. Comparison of mean age, weight, duration of anaesthesia and dose of fentanyl between group A and group B. The ranges of the results are shown in brackets

	Group A	*Group B*
Mean age (years)	32.1 (20–53)	32.5 (19–42)
Mean weight (kg)	59.1 (47–85.7)	56.7 (45–80)
Mean duration of anaesthesia (minutes)	39.5 (20–94)	38.0 (18–70)
Mean fentanyl dose (μg)	115.4 (100–160)	117.6 (90–150)

Table 2. The number of patients in each group who were nauseated or vomited at any time

	Group A ($n = 41$)	Group B ($n = 46$)
Nausea	20	20
Vomiting	20	8*

*$p < 0.005$.

Table 3. Comparison of the number of patients in each group who vomited in the recovery room or in the ward

	Group A ($n = 41$)	Group B ($n = 46$)
Recovery room	12	2*
Ward	17	8**

*$p < 0.005$; **$p < 0.05$.

Table 4. The number of patients requiring postoperative papaveretum with prochlorperazine. The requirements of prochlorperazine alone are given in brackets

	Recovery room	Ward
Group A	11 (1)	3 (2)
Group B	9 (1)	7 (1)

was not significant ($0.05 < p < 0.1$).

In group A, three patients developed bradycardia (defined as a heart rate of less than 50 beats/minute). One patient had second degree heart block at 40 beats/minute and reverted to sinus rhythm after two doses of atropine 0.25 mg intravenously. Another required no treatment and the third patient had a satisfactory blood pressure until neuromuscular blockade was reversed when the heart rate decreased to 40 beats/minute and a further dose of atropine 0.5 mg intravenously was required.

Two patients in group B developed bradycardia. The first was self-limiting with a stable blood pressure but the second patient required 0.75 mg atropine intravenously. A third patient in this group developed a supraventricular tachycardia at 145 beats/minute with a systolic blood pressure of 120 mmHg and normal end tidal carbon dioxide. This reverted spontaneously to sinus rhythm at 105 beats/minute.

Intubating conditions were good at 120 seconds in all patients included in the study, except for one patient who required a further 0.04 mg/kg vecuronium. There were no complaints of awareness in either group. Five patients in group A and two in group B vomited several times postoperatively.

Discussion

Vomiting is a serious side effect of anaesthesia and surgery. It is especially dangerous in the early recovery period when the patient may be drowsy and have suppressed laryngeal reflexes which may allow aspiration of vomitus.[1] It is important, therefore, to develop an anaesthetic technique which is associated with a low incidence of postoperative vomiting.

In the present study, the unexpectedly high incidence of nausea in both groups may be attributed in part to the use of fentanyl peroperatively. A recent study demonstrated an incidence of nausea of 60 percent when using a technique incorporating fentanyl and nitrous oxide for outpatient laparoscopy.[8] Palazzo and Strunin[9] considered that the advantages offered by peroperative fentanyl in respect of cardiovascular stability and reduced postoperative analgesia requirements outweigh the disadvantages of increased emesis. However, in the present study there was no difference in the mean dose of fentanyl in group A and group B (Table 1), suggesting that it was not responsible for the difference in the incidence of vomiting between the two groups.

We deliberately omitted a routine anti-emetic. No single drug appears to be totally effective against emesis and an incidence of 17–21 percent postoperative vomiting persists even when an anti-emetic is used routinely.[10,11] In the present study, surprisingly little postoperative medication was required (Table 4) even by patients with fairly prolonged vomiting.

Nitrous oxide is recognised as having central and peripheral actions which may cause vomiting.[1,7] It has been shown that the effects of nitrous oxide in anaesthetic concentrations are reversed by naloxone which implies interaction with opioid receptors.[12] Gillman[7] suggests that nitrous oxide shares the emetic properties of the opiates. The peripheral effects of nitrous oxide, which may produce nausea and vomiting, include increased middle ear pressure[13,14] and distension of the gastrointestinal tract.[1] Thomsen *et al.*[13] demonstrated a rise in middle ear pressure in a normal subject breathing nitrous oxide. The rate of rise of middle ear pressure varied with the concentration of nitrous oxide inhaled. The time taken for the pressure to reach 2.0 kPa was just over 20 minutes with 80 percent nitrous oxide but more than 50 minutes with 40 percent nitrous oxide. The subject vomited when his middle ear pressure reached 3.4 kPa on one occasion and 2.2 kPa on another. Davis *et al.*[15] demonstrated that the maximum middle ear pressure (2.3–4.2 kPa) was reached after 30–40 minutes anaesthesia using 67 percent nitrous oxide. In the present study, 66 percent of patients in group A and 63 percent of patients in group B underwent anaesthesia for 30 minutes or longer.

Distension of the gastrointestinal tract occurs to a varying degree when performing manual ventilation of the lungs prior to intubation, and also by diffusion of nitrous oxide into the bowel lumen during anaesthesia. The former was avoided in the present study by pre-oxygenating the patients in the place of manual ventilation.

It may be argued that the difference in incidence of vomiting observed was due to a disparity in the depth of general anaesthesia experienced by the groups. In order to achieve approximately equivalent levels of anaesthesia in both groups, we used 1.25 MAC end tidal enflurane.[16] The MAC of enflurane for patients aged 20–55 years has been demonstrated to be 1.68 percent.[16] Adding 70 percent nitrous oxide to the anaesthetic technique reduces the MAC by approximately 66 percent.[16]

Thus, group A received 0.7 percent end tidal enflurane and group B received 2.1 percent end tidal enflurane. There were no complaints of awareness during anaesthesia in either group. Other studies[8,17] in which an inhalational agent was not used have reported awareness in 12 percent and 7.6 percent of patients respectively.

The time from termination of the anaesthetic until the patients regained consciousness was not measured, but subjectively it seemed that group B, which received 2.1 percent enflurane in oxygen and nitrogen, took longer to recover. It may be possible that this accounts for the reduced incidence of vomiting in this group in the recovery room,[18] but the difference persisted on the ward when this effect would no longer be operative. We avoided the use of a Guedel airway to eliminate the retching and gagging which may be induced in some patients on emergence from general anaesthesia.[19] Peroperative hypoxia may influence postoperative vomiting,[1] but no patient in the present study became cyanosed at any time.

The dose of vecuronium used (0.1 mg/kg) provided good intubating conditions at 120 seconds. In a recent study, Caldwell *et al.*[20] found unsatisfactory intubating conditions in 42 percent of patients 150 seconds after 0.07 mg/kg vecuronium. There was no difficulty reversing residual neuromuscular blockade in the present study, even in those patients undergoing short procedures. Many patients required an increment of vecuronium, especially those undergoing laparoscopic egg retrieval for *in vitro* fertilisation which tended to take longer than diagnostic or sterilisation laparoscopy. There were a similar number of laparoscopies for egg retrieval in each group; 13 in group A and 11 in group B.

Cardiac dysrhythmias have been previously reported[20] in patients undergoing laparoscopy when vecuronium has been used for neuromuscular blockade. We did not use an anticholinergic drug as part of our anaesthetic technique and the bradycardias described were observed when the peritoneum was stretched or the uterus was manipulated. The cardiovascular system was otherwise stable.

We found that the technique of avoiding nitrous oxide by using oxygen in nitrogen with enflurane produced a significant reduction in the incidence of postoperative vomiting and provided satisfactory anaesthesia with good surgical conditions and patient acceptance.

As the patients in group B received a higher concentration of enflurane than those in group A, an alternative explanation for our findings might be that enflurane has anti-emetic properties. We feel that this is unlikely and it has not been previously reported.

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Anaesthesia, 1986, Volume 41, pages 708–711

Ketanserin and the cardiovascular system

1. Modification of the effects of pressor amines in patients undergoing myocardial revascularisation

H. B. A. GRIFFITHS AND J. G. WHITWAM

Summary

The effect of 10 mg of ketanserin on the pressor responses to noradrenaline, phenylephrine and angiotensin II in 19 patients during cardiopulmonary bypass was observed. The results were compatible with the previously reported evidence that ketanserin, in addition to its antagonism of serotonin, causes alpha$_1$ adrenoceptor blockade.

Key words

Pharmacology; ketanserin.
Sympathetic nervous system; alpha-adrenergic blockade.

Ketanserin is a 5-hydroxytryptamine (5-HT$_2$) antagonist. It is both an arterial and venous vasodilator and, in man, causes a fall in arterial blood pressure.[1-3] When given in the recommended dosage, ketanserin has been shown to have an alpha$_1$ adrenoceptor blocking effect in normal volunteers.[4] Work in animals has shown that blood pressure responses to 5-HT are strongly inhibited by doses of ketanserin 25–100 times less than those required to reduce blood pressure.[5] It has been proposed that further work is necessary to elucidate the precise mechanism of the hypotensive effect of the drug[6] since work in animals suggests that the major factor contributing to the hypotensive effect of ketanserin is not 5-HT$_2$ antagonism but alpha$_1$ adrenoceptor blockade.[6]

In order to investigate further the mode of action of ketanserin, observations of the effect of this drug on the pressor effects of noradrenaline, phenylephrine, and angiotensin II were made in patients undergoing cardiopulmonary bypass.

Methods

The method used in this part of the study was similar to that used previously to study the effect of droperidol on the responses to adrenaline and noradrenaline during cardiopulmonary bypass.[7] Informed consent was obtained for the ethical committee approved study.

Observations were made on 19 patients and their admission criteria and general management were similar to those outlined in a previous paper,[8] except that anaesthesia was induced with midazolam 0.2 mg/kg and thiopentone 2.5–3 mg/kg and the opioid used in maintenance was fentanyl (total dose 35 μg/kg). The study was performed during rewarming, after removal of the aortic cross clamp with a constant perfusion rate (2.4 litres/sq m/minute) and control mean arterial pressures of 47–62 mmHg. The nasopharyngeal

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temperature range during the period in which the observations were made was 34–36°C and, although the heart was beating, it was not yet ejecting.

Phenylephrine ($n = 5$). This was administered in incremental doses of 100, 200 and 300 μg into the perfusion system and the effect on arterial pressure was observed. Ketanserin 10 mg was then administered and the three doses of phenylephrine repeated after an interval of 10 minutes.

Noradrenaline. Here a control group ($n = 5$) was introduced who received no ketanserin. Noradrenaline was administered in doses of 5, 10 and 15 μg into the perfusion system at 4-minute intervals and the effects on mean arterial pressure observed. After 8 minutes, the effect of a second series of the three doses of noradrenaline was observed. In the test group ($n = 6$), ketanserin 10 mg was administered 4 minutes after the third dose (15 μg) of the first series of three doses of noradrenaline (5 μg, 10 μg and 15 μg). The first of the second series of doses of noradrenaline was administered 4 minutes later, so that the intervals between the doses of noradrenaline was the same as in the control group.

Angiotensin II ($n = 3$). The effect of two doses of ketanserin 10 mg administered into the perfusion system was observed on the pressor responses to 50 μg of angiotensin II. The angiotensin was administered into the perfusion system at the time of the maximum depressor response following ketanserin.

Statistical analysis was performed using paired t-tests within groups and unpaired t-tests between groups.

Results

The mean ages and weights of the 19 patients studied in this group were 55.6 (SD 23) years and 75.5 (SD 4.5) kg respectively. The reduction of mean perfusion pressure in response to the injection of 10 mg of ketanserin into the pump oxygenator system varied between 3 and 12 mmHg. However, in most patients, this initial effect was relatively transient, so that partial recovery had occurred by 4 minutes, but in six patients the effect of ketanserin on the mean arterial pressure persisted throughout the period of observation.

Noradrenaline

The mean baseline arterial pressures in the patients who received only noradrenaline and those who also received ketanserin between the doses of noradrenaline were 57 (SEM 2.9) mmHg and 51.3 (SEM 3.1) mmHg, which were not statistically significantly different (Table 1).

The pressor responses to noradrenaline are shown in Table 1. In order to evaluate the modification by ketanserin of the pressor response to noradrenaline, a comparison was made of the difference between the effect of the first and second series of doses of noradrenaline with and without ketanserin, as suggested by Fozard.[5] It can be seen (Fig. 1) that ketanserin caused a marked reduction in the effect of noradrenaline, which was highly significant at all three dose levels; thus, an augmentation was converted to a reduction of its effect and mean differences in response of 6.86, 9.56 and 15.18 mmHg at doses of 5, 10 and 15 μg respectively, all of which were statistically significant ($p < 0.05$).

Phenylephrine

In five patients, the mean responses in mean

Table 1. Changes in mean arterial pressure (SEM) mmHg in response to doses of noradrenaline (NA). Control: response to two series of incremental doses of NA; ketanserin: 10 mg ketanserin administered into the pump oxygenator between the two series of doses of NA.

		Dose of noradrenaline (μg)		
		5	10	15
Control ($n = 5$)	1st series	11.1 (2.86)	19.0 (3.24)	27.1 (4.35)
	2nd series	15.3 (2.04)	25.8 (2.24)	33.1 (3.4)
	p	NS	<0.05	NS
Ketanserin ($n = 6$)	1st series	14.6 (1.43)	23.4 (2.89)	31.3 (3.60)
	2nd series	11.9 (1.13)	17.3 (3.08)	22.7 (4.28)
	p	NS	NS	NS

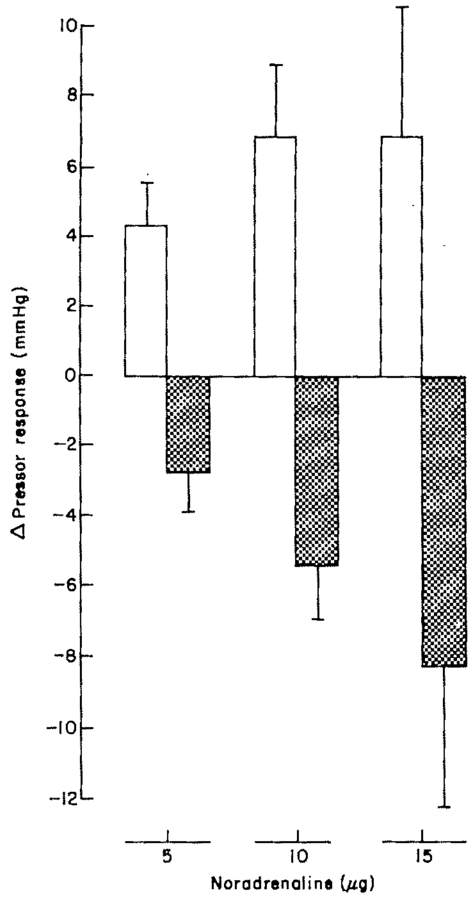

Fig. 1. Effect of ketanserin on pressor responses to noradrenaline (NA); (□), control group ($n = 5$). Difference in pressor response between two series of doses of NA showing a greater response to the second series (i.e. enhancement of effect) (▦), ketanserin group ($n = 6$). Difference in pressor responses to two series of doses of NA in patients in whom ketanserin (10 mg) was injected into the pump oxygenator between the two series of doses showing a reduction of the pressor effect of NA. The difference between the control group and the ketanserin group was statistically significant. ($p < 0.05$ for each dose). Bars: 1 SE (figure constructed from data in Table 3).

arterial pressure of doses of 100, 200 and 300 μg of phenylephrine were 8.08 (SEM 1.33) 13.9 (SEM 2.89) and 20.7 mmHg respectively. After ketanserin, the comparable responses were 7.73 (SEM 2.07) 12.5 (SEM 2.8) and 16.6 (SEM 3.77) mmHg, which although less, were not statistically significantly different from the control values.

Angiotensin II

Ketanserin appeared to have no significant effect on the response to doses of 50 μg of angiotensin II. In Fig. 2, the absence of an effect of 20 mg of ketanserin (10 mg repeated within 3 minutes) on the pressor response to 50 μg of angiotensin II is clearly illustrated.

Discussion

It has been demonstrated previously that the repeated administration of noradrenaline results in an increasing pressor effect[5] and this has been confirmed in man in this study. The ability of ketanserin to abolish this effect has also been demonstrated and there is a highly statistically significant difference between the study and control groups in the dose response study with noradrenaline (Fig. 1). A similar, although not statistically significant, reduction in the pressor effect of phenylephrine was shown, which is in keeping with previous work.[5,9] The lack of an effect of ketanserin upon the pressor effects of angiotensin II is in accordance with the view that it exerts its effects through blockade of alpha$_1$ adrenoceptors, or a modification of the amplifier effect of serotonin on adrenergic responses.[5] The elimination half life of ketanserin is thought to be around 15 hours[10] and, as mentioned above, in some patients its effects persisted throughout the period of study.

In conclusion, ketanserin antagonises both the

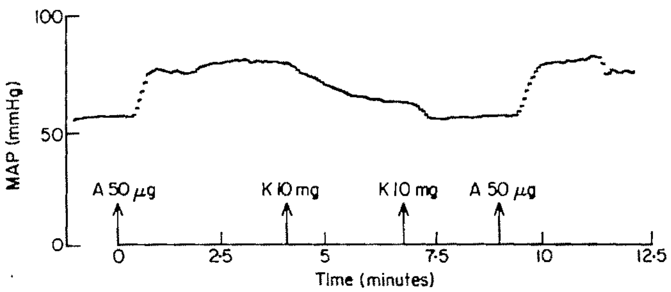

Fig. 2. Effect of ketanserin (K) on pressor response to angiotensin II (A). Mean arterial blood pressure (MAP) continuous record of arterial pressure radial during cardiopulmonary bypass. Drugs injected into the oxygenator at the times indicated by the arrows.

effects of noradrenaline and phenylephrine, which is in keeping with the view that it blocks alpha_1 adrenoceptors. In addition, it abolishes the amplification of the pressor response seen with repeated doses of noradrenaline, in which serotonin has been implicated as a mediator. However, the relative contribution of these two mechanisms to the pharmacological effects of the drug has not yet been definitely established and further studies would seem to be merited.

Acknowledgments

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Ketanserin and the cardiovascular system

2. A study of its effects in patients undergoing myocardial revascularisation

H. B. A. GRIFFITHS AND J. G. WHITWAM

Summary

A double-blind study was performed on 19 patients undergoing myocardial revascularisation. Rou anaesthetic and cardiopulmonary bypass procedures were used. Nine patients received ketanserin continuous infusion and ten received an equal infusion rate of placebo. Arterial blood pressure was contro with sodium nitroprusside. The ketanserin group had a significantly higher cardiac index and a lo peripheral vascular resistance during the first 2 hours after bypass.

Key words

Anaesthesia, cardiovascular.
Pharmacology; ketanserin.

Ketanserin, a quinazoline derivative, is a new, selective 5-hydroxytryptamine (5-HT_2) antagonist. It is both an arterial and venous vasodilator and, when given intravenously in man, causes a fall in both systolic and diastolic arterial blood pressure.[1-3] Like some other quinazoline derivatives, it possesses $alpha_1$ adrenoceptor blocking qualities and is also a weak antagonist at the H_1 histaminergic site.[2] It has been used to control blood pressure in a wide variety of clinical situations and, in particular, has been used, either by infusion or by bolus injections, as the sole agent to control peri-operative hypertension in patients undergoing coronary artery bypass surgery.[4-6] Between 15 and 80% of patients undergoing myocardial revascularisation develop peri-operative hypertension[7] and the effectiveness of ketanserin in controlling this has prompted the suggestion that 5-HT plays an important role in the genesis of hypertension associated with this type of surgery.[4] However, more recently An and Prys-Roberts[8] found that plasma seroto concentrations did not appear to be related the hypertension seen in patients underg coronary artery surgery.

In order to investigate further the hae dynamic effects of ketanserin, a double bl study was performed on patients underg cardiac surgery.

Methods

Observations were made on 19 patients (15 m 4 female) undergoing coronary artery surgery. had given their informed consent to the st which had been approved by the local eth committee. Entry criteria were patients pres ing from the waiting list, less than 65 year age, good left ventricular function (assessed exercise tolerance), a normal left ventricular

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diastolic pressure and ejection fraction and the absence of significant measurable dysfunction of other systems. Exclusion criteria were inadequately controlled pre-operative hypertension, impaired left ventricular function and evidence of serious multisystem disorders. All patients were receiving atenolol (dose range 100–200 mg daily and had resting heart rates around 70 beats/minute.

After overnight sedation with lorazepam (3–5 mg oral), the patients received papaveretum (15–20 mg) hyoscine (0.3–0.4 mg) and droperidol (5 mg) intramuscularly 60–80 minutes before the induction of anaesthesia. On arrival in the induction area, an ECG recording was started and a peripheral venous infusion and arterial pressure measurement were set up using local anaesthesia.

Anaesthesia was induced with thiopentone 4 mg/kg, papaveretum 0.6 mg/kg in divided doses, pancuronium 0.12 mg/kg and maintained after tracheal intubation during artificial ventilation of the lungs with nitrous oxide (60%) in oxygen and further doses of papaveretum and pancuronium, 0.2 mg/kg and 0.04 mg/kg respectively. Gentamycin 80 mg and flucloxacillin 500 mg were administered intravenously at the start of surgery.

Measurements

After the induction of anaesthesia, a flow directed thermodilution catheter (Gould Medical) was positioned in the pulmonary artery through a valved introducer placed in the right internal jugular vein. After wedging the catheter during its introduction, no further measurements of wedge pressure were made. Primary measurements were systemic and pulmonary arterial and central venous pressures, heart rate and cardiac output. Systemic vascular resistance was calculated in dynes/second/cm^{-5} (i.e. mean arterial pressure – mean central venous pressure × 79.9/cardiac output) and cardiac index in litres/sq m/minute. PaCO$_2$ and arterial pH were measured and maintained within normal limits throughout. The PaO$_2$ was between 13 and 20 kPa before bypass, in excess of 25 kPa during bypass and between 9.5 and 16 kPa after bypass. Potassium was administered to maintain a value between 4.5 and 5.5 mmol/litre. Central temperature was measured in the nasopharynx throughout and skin temperature (toe) was also measured postoperatively. After the induction of anaesthesia, a urinary catheter was passed and urine output was measured during surgery and postoperatively. Frequent measurements of haematocrit were made.

Cardiopulmonary bypass was established using a standard procedure with a bubble oxygenator and a crystalloid prime with an initial cardiac index of 2.4 litres/sq m/minute at 37°C. The patients were cooled to 27°C, when the perfusion rate was reduced to 1.52 litres/sq m/minute. After occlusion of the aorta, 1 litre of cardioplegia solution (St Thomas') between 0°C and 4°C was administered via the aortic root. During rewarming, the cardiac index was progressively increased to 2.4 litres/sq m/minute.

Ketanserin

The drug was presented in 10 ml ampoules containing 5 mg/ml. The patients were allocated to two groups. Group A ($n = 9$) received ketanserin as an infusion of 0.06 mg/kg/hour (approximately 4.5 mg/hour). Group B ($n = 10$) received the solvent alone (50 mg dextrose, 3 mg tartaric acid, 0.05 mg propylene glycol, water q.s. with sodium hydroxide q.s. to pH 3.4) at the same volumetric rate (0.012 ml/kg/hour). In both groups, the infusion rate was doubled to 0.024 ml/kg/minute during cardiopulmonary bypass and returned to 0.012 ml/kg/hour at the end of bypass, as suggested by previous workers.[4] The drug and solvent alone were supplied blind and randomised with serial numbers and a code which could be broken if required.

After induction of anaesthesia, when stability had been achieved and baseline measurements obtained, the infusion of the test solution was commenced and subsequently continued throughout. The study was terminated 4 hours after the end of cardiopulmonary bypass.

After control measurements, cardiac output was measured at the following times: the start of the infusion of test material, immediately before the skin incision, pre- and poststernotomy, prebypass and thereafter every 30 minutes for 4 hours.

Control of arterial pressure

None of these patients required inotropic agents. The aim was to maintain systolic arterial pressure between 105 and 130 mmHg in the prebypass and postoperative periods. During cardiopulmonary bypass, the baseline mean arterial pressure was not allowed to increase above 65–70 mmHg.

In the prebypass period, arterial pressure was controlled with halothane. After this period, any tendency of the blood pressure to rise above the predetermined limits was controlled entirely with sodium nitroprusside administered in a strength of 50 mg in 50 ml using a Vickers infusion pump. Each 30 minutes, the consumption of nitroprusside was observed and the infusion rate calculated in μg/minute/kg. All the patients required nitroprusside at some stage of their management.

In addition to the pump prime, 1–2 units of whole blood were transfused in the postoperative period.

Statistical analysis was performed using two-way analysis of variance followed by unpaired *t*-tests.

Table 1. Age, weight, surface area, number of coronary grafts, duration of cardiopulmonary bypass and time from the induction of anaesthesia to transfer to the intensive care unit. Mean (SEM).

	Ketanserin group ($n = 9$)	Control group ($n = 10$)	
Age (years)	54.0 (2.92)	54.9 (1.99)	NS
Weight (kg)	86.5 (3.30)	83.0 (3.45)	NS
Surface area (sq m)	2.02 (0.04)	1.96 (0.04)	NS
Number of grafts	3.56 (0.29)	3.40 (0.31)	NS
Duration of bypass (minutes)	82.8 (6.9)	90.0 (7.5)	NS
Time from induction of anaesthesia to transfer to intensive care (minutes)	173.0 (12.7)	174.0 (10.0)	NS

Results

There were no significant differences between the two groups in age, weight, surface area, number of coronary grafts, duration of bypass and the time from the induction of anaesthesia to transfer of the patients from the operating theatre to the intensive care unit. (Table 1).

Sodium nitroprusside. The times from the induction of anaesthesia to the first use of this vasodilator were 48.9 minutes (SEM 13.1) and 53.5 minutes (SEM 18.4) in the ketanserin and control groups respectively. There were no statistically significant differences in the rate of administration of sodium nitroprusside between the groups, either during cardiopulmonary bypass or during the first, second, third and fourth hours after bypass. The rates of administration varied between 0.2 μg/kg and 2.3 μg/kg/minute during cardiopulmonary bypass and 0.6 μg/kg/minute and 5.5 μg/kg/minute during the first 4 hours after bypass.

Serum potassium. This was in the range 4.5–5.2 mmol/litre throughout and there were no significant differences between the two groups of patients.

Haematocrit. There were no significant differences between the two groups. The mean preoperative values were 38.2% (SEM 0.5) and 37.7% (SEM 0.4) in the ketanserin and the control groups respectively, falling to minimum mean values of 26% (SEM 0.9) and 25% (SEM 0.7) respectively during cardiopulmonary bypass. The mean values in the ketanserin and control groups at 1, 2, 3 and 4 hours post bypass were 31% (SEM

Table 2. Systemic arterial pressure (mmHg) and heart rate (beats/minute) in the ketanserin ($n = 9$) and control groups ($n = 10$). Mean (SEM) CPB- Cardiopulmonary bypass

		Arterial pressure					
		Systolic		Diastolic		Heart rate	
		Ketanserin	Control	Ketanserin	Control	Ketanserin	Control
Pre-ketanserin or placebo infusion		128.9 (11.1)	127 (5.4)	74.4 (5.3)	75.0 (3.4)	62.2 (3.7)	73.0 (4.2)
15 minutes after start of infusion		106.7 (5.5)	123 (5.6)*	62.2 (4.6)	72 (4.4)	70 (4.4)	75.5 (2.2)
Lowest pressure recorded During CPB		43.9 (4.4)	37.8 (3.5)	—	—	—	—
Post CPB	10 minutes	107.8 (4.3)	122 (4.6)*	57.8 (1.5)	65.0 (2.9)*	77.2 (4.5)	83 (4.1)
	1 hour	114.4 (3.4)	122 (5.2)	63.3 (2.4)	66.5 (3.7)	75.6 (6.7)	86.5 (3.0)
	2 hour	120.0 (3.3)	121.5 (3.9)	66.7 (1.7)	70.5 (1.6)	83.3 (5.8)	83.5 (4.8)
	3 hour	126.7 (4.4)	129.5 (5.2)	74.4 (2.4)	72 (1.9)	91.1 (7.5)	88.5 (4.9)
	4 hour	120.0 (5.0)	127.0 (4.0)	70.0 (3.3)	60 (2.2)	86.7 (5.5)	89.0 (3.6)

*$p < 0.05$. For all other values there were no significant differences between ketanserin and control groups.

0.9) and 30.1% (SEM 1.1), 32.5% (SEM 0.9) and 33% (SEM 1.08), 33.8% (SEM 0.7) and 34.1% (SEM 0.5) and 34.2% (SEM 0.6) and 34.0% (SEM 0.45) respectively; there were no statistically significant differences between the two groups.

Arterial pressure. (Table 2). Compared with the control group, the ketanserin treated patients showed the following statistically significant differences: a lower mean systolic arterial pressure 15 minutes after starting the infusion of the drug (mean 106.7 mmHg compared with 123 mmHg $p<0.05$), lower mean systolic (107.8 mmHg compared with 122 mmHg $p<0.05$) and diastolic (57.8 mmHg compared with 65 mmHg $p<0.05$) pressures immediately after cardiopulmonary bypass.

Heart rate (Table 2). There were no significant differences between the two groups.

Cardiac index (Fig. 1). One hour after ending cardiopulmonary bypass the ketanserin group had a 23% greater mean cardiac index of 3.05 litres/sq m/minute compared with 2.48 litres/sq m/minute in the control group ($p<0.01$).

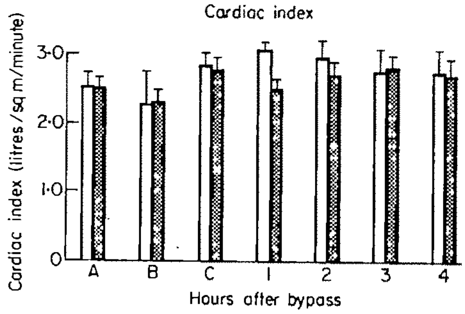

Fig. 1. Cardiac index (□), Ketanserin ($n=9$; (▨), control ($n=10$). Bars, 1 SEM (A) After induction of anaesthesia before the start of the ketanserin or placebo infusion. (B) Immediately before cardiopulmonary bypass. (C) 10 minutes after bypass.

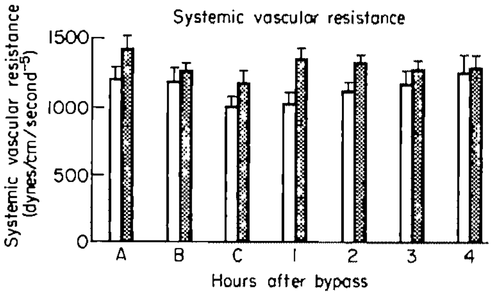

Fig. 2. Systemic vascular resistance (□) Ketanserin ($n=9$); (▨) control ($n=10$). Bars, 1 SEM. (A) After induction of anaesthesia before the start of the ketanserin or placebo infusion; (B) immediately before cardiopulmonary bypass; (C) 10 minutes after bypass.

Systemic vascular resistance (Fig. 2). The mean peripheral vascular resistance was 24% (1016 dynes/cm/second^{-5} compared with 1336 dynes/cm/second^{-5}, $p<0.005$) and 16% (1100 dynes/cm/second^{-5} compared with 1314 dynes/cm/second,$^{-5}$ $p<0.005$) less at 1 and 2 hours post-bypass respectively in the ketanserin-treated group.

Pulmonary artery pressure. Except during the prebypass period, pulmonary arterial pressures were within the normal range in both groups throughout.

Discussion

On the basis of previous work,[3,4] caution was exercised in the choice of the ketanserin dosage for this study. The investigators were constrained to this regimen by the double blind design of the trial and the need to avoid hypotension during the pre-operative period and also during cardiopulmonary bypass. The anaesthetic technique was deliberately chosen to provide adequate hypnosis throughout, while causing minimal suppression of somatosympathetic reflexes so that strict control of arterial blood pressure required additional measures to be taken, and all the patients required sodium nitroprusside at some time during the study period. It seems that the effects of this low dose infusion of ketanserin were masked by this aspect of anaesthetic management and that sodium nitroprusside made the major contribution to blood pressure control, so that there was no significant difference in the rate of administration of sodium nitroprusside between the two groups.

Nonetheless, the results clearly show an improvement in certain cardiovascular variables in the ketanserin group compared with the controls; in particular, there was an increase as high as 23% in mean cardiac index (Fig. 1) and a decrease of 24% in mean systemic vascular resistance (Fig. 2) without any difference in heart rate during the first 2 hours after bypass. During this time there were no differences in haematocrit between the two groups, which could have explained these observations. Thus, the ketanserin-treated group had a more desirable haemodynamic profile in the imediate post-operative period. The diminution of this favourable effect after the first 2 hours after bypass is probably due to a reduction in the level of analgesia and neuromuscular blockade with pain and shivering and may be a further consequence of the low dose of ketanserin used.

Ketanserin causes a reduction in arterial blood pressure without an associated tachycardia. This is reminiscent of the effects of opioids, where the suggestion has been made that baroreceptor sensitisation results in a vagally-mediated reflex causing a reduction in heart rate.[9] There seems little evidence to implicate this, however, in the case of ketanserin, which crosses the blood–brain barrier only in small amounts.[10] Another possible explanation of the absence of a reflex tachycardia during hypotension induced with ketanserin, is that it has a direct effect on the heart, in particular the sino-atrial node. Whatever the mechanism, this feature makes ketanserin a potentially valuable agent where blood pressure control is required and a large increase in heart rate is undesirable.

Although the dose of ketanserin chosen for this study is considered to be low, the evidence presented suggests that the drug might be a useful adjuvant to afterload control. Its elimination half life of around 15 hours[11] would allow its use as a background drug in concert with other agents.

In conclusion, ketanserin lowers arterial pressure without causing a tachycardia and the drug merits further study, particularly in the control of hypertension in patients with coronary artery disease.

Acknowledgments

We wish to thank Mr R.H. Sapsford and Mr R. Stanbridge for permission to study these patients. Janssen Pharmaceutical supported this work by providing the coded drug and placebo and funding the purchase of the disposables required for the measurement of cardiac output.

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Anaesthesia, 1986, Volume 41, pages 717–720

Pupil response to alfentanil and fentanyl

A study in patients anaesthetised with halothane

A. J. ASBURY

Summary

The pupillary response to alfentanil, fentanyl and a saline placebo was measured in patients anaesthetised in a standard manner with halothane, to determine whether the pupil diameters changed in a way which could be distinguished from background activity. Measurements were made to the nearest 0.1 mm using a purpose-built pupillometer. The response to the drugs can be clearly distinguished from the background activity seen in the placebo group. The time courses of constriction caused by the two drugs are significantly different from the placebo group responses. The time to maximum to response with alfentanil is 4 minutes compared with 8 minutes for fentanyl. Both drugs produced at least 35% reduction in mean pupil diameter compared with the placebo group. The duration of the response to alfentanil was 25 minutes, whereas the fentanyl response lasted more than one hour.

Key words

Analgesics; alfentanil, fentanyl.
Measurement techniques; pupillary response.

Many anaesthetists look at the pupils during an operation, but the changes in pupil diameter (PD) can be difficult to interpret. The problem is that the PD has a range of normal physiological responses and, in addition, responds to many anaesthetic drugs.

There are many physiological features which change PD. For example, it decreases with age, reaching a minimum at about 60 years. Furthermore, the pupil diameter is constantly changing, even in steady light, and this is thought to be a response to the imbalance between sympathetic and parasympathetic tone. Iris colour affects the duration and rate of response, particularly with topically applied drugs. Dark eyes respond more slowly than lighter eyes to parasympatholytics such as cyclopentolate.[1] Perhaps the most important changes in PD arise from emotion, particularly fear, anxiety and pain.

Many drugs used in anaesthesia change PD and their effects can be very long lasting. Mirakhur,[2] in his study of atropine and hyoscine, showed that the PD could change from a mean of 4.3 mm to more than 7.0 mm in 6 hours following 1.0 mg of intramuscular hyoscine and from 3.5 mm to 5.5 mm following 2.0 mg of intramuscular atropine.

In 1981, Larson described the effects on PD of thiopentone bolus doses given over 15 seconds to age-matched groups of ASA 1 patients.[3] In unpremedicated patients, thiopentone 4 mg/kg increased the PD by up to 25% at one minute; this returned to pre-injection values by 3 minutes. In patients premedicated one hour

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before the 4 mg/kg bolus with promethazine, pethidine and atropine, the PD was smaller and decreased further, reaching 80% of its former diameter at 2 minutes.

Balamoutsos and his colleagues investigated the reversal of neuromuscular blockade with neostigmine 28 μg/kg and atropine 1.4 μg/kg in one hundred fit patients.[4] They concluded that under nitrous oxide and fentanyl anaesthesia, neither atropine nor neostigmine significantly altered PD, and that after reversal the biggest PD change occurred when the nitrous oxide was discontinued. The PD may also be altered by many other drugs including morphine, pethidine, ergometrine, trimetaphan, adrenaline, carbachol, ephedrine, dexamethasone, histamine and nalorphine.[5]

The PD may be altered by so many factors associated with anaesthesia, so the author was interested to discover if anaesthetists still looked at pupils and how they interpreted what they saw. A brief survey of 42 anaesthetists from all regions of the country showed that all but four looked at the pupil regularly, but none could describe a sequence of changes that they expected in relation to the progress of an anaesthetic.

The objective of this study was to quantify the normal PD activity during a standard anaesthetic technique and then to measure the changes following intravenous injections of fentanyl or alfentanil.

Methods

Thirty-one consecutive ASA 1 patients undergoing routine abdominal surgery gave written consent (using a proforma approved by the local ethical committee) for pre-operative eye examination and pupillometry during anaesthesia. Seven patients with eye defects (including myopia) were excluded from the series at the initial examination.

Of the remaining 24 patients, none was receiving drug treatment apart from antibiotics and subcutaneous heparin. All had normal blood biochemical and haematological values. Thirty millilitres of aluminium hydroxide were given orally 30 minutes before induction in each case, and no opiates or antisialogogues were given.

The patients were randomly divided into three groups of eight and allocated to receive either saline, alfentanil 6 μg/kg or fentanyl 2 μg/kg, doses commonly used to supplement anaesthesia. The author did not know the identity of the drug until after the study.

After an intravenous infusion of Hartmann's solution, the patient was pre-oxygenated, anaesthesia was induced with methohexitone 0.1 mg/kg and tracheal intubation was facilitated with suxamethonium 0.6 mg/kg. The lungs were then inflated with nitrous oxide, oxygen and halothane, and pancuronium 0.1 mg/kg was given. In theatre, the lungs were ventilated using a Manley ventilator, and 2% inspired halothane was given for 10 minutes. The concentration was then reduced to 0.5% and subsequently adjusted according to the patient's response to surgical stimulation. We did not have the equipment to measure end tidal halothane concentrations. The blood pressure was measured at 5 minute intervals, using an automated recorder (Dinamap, Critikon). The ventilation was adjusted to give an expired carbon dioxide concentration of 3.8–4.2% (Normocap, Datex).

Once surgery had started, the left PD was measured at 2-minute intervals, using the previously described, calibrated pupillometer[6] under controlled lighting conditions; all the measurements were made by the author. The measurements were continued until a steady state had been achieved, which was defined as systolic arterial pressure within 15% of the admission value, pulse rate above 60 and below 100 beats/minute, absence of sweating or lacrimation, pupil diameter between 2.5 and 4.0 mm, and the PD range during any three consecutive measurements not exceeding 0.2 mm. The mean of these three measurements was called the pre-injection PD. When this state had been achieved, no further alterations to the inspired halothane concentration were made.

The test substance, made up to 5 ml, was then injected over 30 seconds into a fast-running infusion. Pupil diameter measurements were made at 2, 4, 6, 8, 10, 15, 20, 25, 35, 45, 55 and 65 minutes from injection, as long as the anaesthetic lasted or until the PD had returned to the pre-injection value.

The Mann-Whitney U test was used to examine the significance of the differences in PD between the groups at each time point. A probability value of less than 0.05 was considered to be significant.

Results

Four patients in the placebo group had blue or

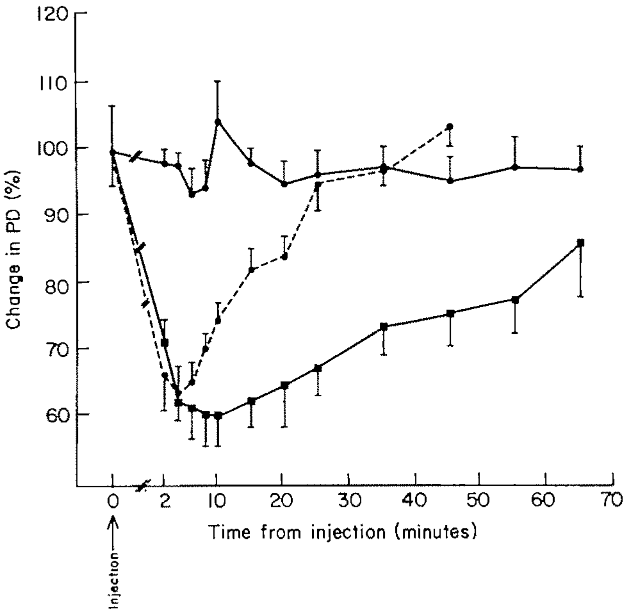

Fig. 1. Graph showing the time courses of the pupil diameter (PD) changes following injections of saline, alfentanil 6 μg/kg or fentanyl 2 μg/kg. The results are expressed as percentages of the steady state pre-injection PD, with standard errors. ■—■, Fentanyl; ●——●, alfentanil; ●——●, placebo.

light eyes. Five patients in the fentanyl group had blue or light eyes and three in the alfentanil group.[5]

There were no significant differences between the mean ages of the patients in the placebo group, 44.9 years (SD 17.0) the fentanyl group, 55.6 years (SD 11.9) and the alfentanil group, 49.7 years (SD 8.4). There were no significant differences between the mean weights of the patients in the placebo group 65.7 kg (SD 7.0), the fentanyl group 63.7 kg (SD 7.8) and the alfentanil group 65.7 kg (SD 7.6). There were also no significant differences between the mean pre-injection PDs in the placebo group 3.0 mm (SD 0.48) the fentanyl group 2.9 mm (SD 0.57) and the alfentanil group 3.1 mm (SD 0.49). The overall mean was 3.0 mm (SD 0.49).

The PD's for the three groups are expressed as a percentage of the pre-injection value and plotted in Fig. 1. In the placebo group, the PD was below 100% except at the 10-minute point. The alfentanil response is at a maximum at 4 minutes, whereas the fentanyl response reached its maximum at 8 minutes. Each drug produced at least a mean decrease in PD of 35%. The fentanyl response is statistically significantly ($p<0.05$) different from the placebo response from 2 to 65 minutes, whereas the alfentanil group differed significantly from the placebo group from 2 to 20 minutes. The responses after fentanyl and alfentanil are significantly different from each other from 6 to 25 minutes.

Discussion

The results suggest that once the steady state defined above has been reached in the placebo group, large changes would not be expected thereafter. Many of the transient changes, for example, when a surgeon pulls on the mesentery, have cancelled out in the calculation of the means.

The time courses of the PD responses in the fentanyl and alfentanil groups are significantly different from the placebo group PDs and from each other. The changes in PD are small, from a mean starting diameter of 3.0 mm which decreased at peak effect to nearly 2.0 mm. These changes can be seen by the naked eye but, for accurate measurement (within 0.2 mm), a microscope, a calibrated scale and standardised lighting was needed.

The results of this study suggest that fentanyl and alfentanil may have different miotic potencies, since fentanyl 2 μg/kg and alfentanil 6 μg/kg produce approximately the same change in PD. It is difficult to draw more precise conclusions without information on the blood concentrations particularly as the drugs may be acting on the iris by several different mechanisms.[5]

The morphine-type mechanism prevents the cortical inhibition of the Edinger-Westphal nucleus, but direct effects on the iris are also possible. The drugs may gain access to the iris in three ways: bloodborne (the iris has a rich blood supply), the drugs might also be excreted in tears and affect the iris via the tear screen and they may be excreted in the aqueous humor. This is particularly possible with fentanyl, because of its high lipid solubility.

This study shows clear evidence of pupillary activity during surgical anaesthesia, and the miotic responses to alfentanil and fentanyl can be clearly distinguished from this. The changes are small and difficult to see unaided.

Acknowledgments

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The anaesthetist and the obstetric flying squad

Could complacency creep in?

C. C. CALLANDER AND P. HUTTON

Summary

The demands made upon the Bristol obstetric flying squad over the past 14 years have been analysed. During this period, the number of calls received per year has decreased dramatically. The reasons for this are discussed in the context of current obstetric practice. The management of retained placenta is reviewed. Of importance to anaesthetists is the gross reduction in the number of cases where it is necessary to give anaesthesia 'in the field'. This may lead to complacency and lack of familiarity with the equipment carried by the flying squad.

Key words

Anaesthetic; obstetric, emergency.
Complications; resuscitation.

It is now well over 50 years since the first obstetric flying squad was set up in Bellshill, Lanarkshire, following a suggestion by the late Professor E. Farquhar Murray that '... instead of rushing a shocked and collapsed patient to hospital for nursing and specialist aid, the specialist and nurse should be rushed to the patient'.[1] Now, most parts of the United Kingdom are covered by flying squads based at consultant obstetric units and they serve those patients electing to deliver at home or in a General Practitioner maternity unit (GP unit).

Over the past decade, the need for an obstetric flying squad has been questioned on several occasions. Not only has the number of cases dealt with been reported as falling,[2] but also the time taken for a normal ambulance to collect patients and return them to hospital is significantly less than that taken by the flying squad to assemble staff, load equipment and make the outward journey.[2,3] In addition, the type of case to which the squad is now called has changed and high numbers of unjustified calls have been reported.[2,3] Changes to the service that have been suggested include, either its replacement with a general purpose mobile resuscitation unit,[4] or its total abolition in urban areas.[3] The present service, however, has been defended repeatedly,[5,6] and in 1979 the General Medical Services Committee adopted a recommendation of the Maternity Services Sub-Committee that '... it is essential that flying squads or appropriate emergency services should be available in all areas'.[7]

Most reviews of obstetric flying squad services have restricted their observations to the obstetric component and have provided little detail of the anaesthetic contribution,[2,3,5] despite the fact that the anaesthetic has been described as the 'least perfect and perhaps the most dangerous aspect of a flying squad call'.[8] Because of this, it was decided to analyse the anaesthetic demands

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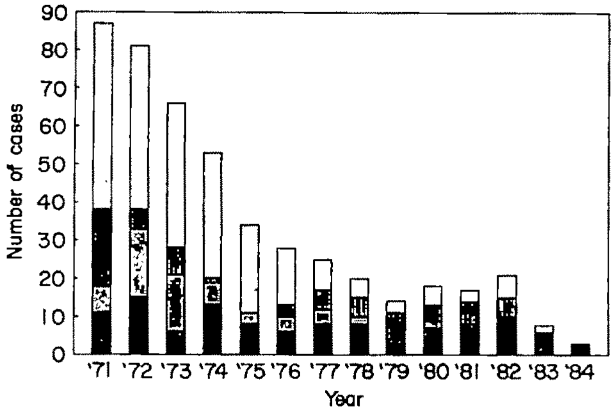

Fig. 1. Demands made upon the Bristol flying squad 1971–84. Reasons for call: (□). retained placenta; (▤), antepartum haemorrhage; (▥), postpartum haemorrhage not associated with retained placenta; (■), pre-eclampsia and eclampsia; (■), other causes.

placed on our own flying squad in the light of past and present obstetric policies. In particular, it was hoped to assess what effects, if any, current obstetric policies were having on the role of the anaesthetist and his training.

The work of the flying squad

The obstetric flying squad in Bristol is based at Southmead Hospital and covers an area roughly within a 20-mile radius. The total number of deliveries within this region is approximately 10 000 per year. The flying squad team always includes an anaesthetist (registrar, senior registrar or consultant), an obstetrician (registrar, senior registrar or consultant) and an experienced midwife. In specific instances, where the fetus or newborn is known to be in difficulty, a paediatrician is also included. After each call, a record is made of the case details, the treatment given and the eventual outcome. These records were analysed for the 14-year period 1971–1984 with regard both to the overall work of the flying squad and to the anaesthetic contribution. All the calls received came from either the patient's home or a GP unit.

Figure 1 shows the total number of requests for urgent assistance each year, subdivided into the reasons for call out. Figure 2 shows the number of anaesthetics given each year in the place to which the flying squad was called. The reasons for the anaesthetics are shown as subdivisions of the bar graphs. Throughout the whole 14-year period, 216 general and three spinal anaesthetics were administered.

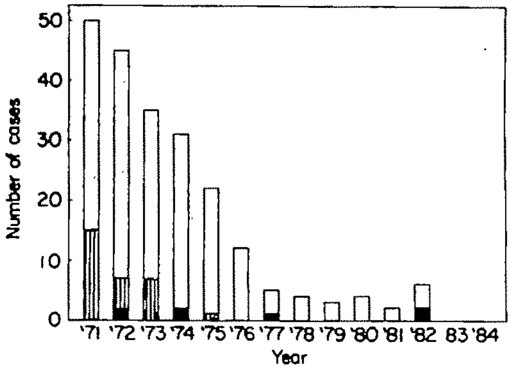

Fig. 2. Anaesthetic procedures carried out by the Bristol flying squad at the place of confinement. Anaesthesia required for: (□), retained placenta; (▥), postpartum haemorrhage not associated with retained placenta; (■), other.

The changing pattern of confinement

Detailed figures for the place of confinement in the Bristol area are only available from 1976 onwards, due to the administrative reorganisation of the National Health Service in 1974. Table 1 shows the breakdown of the place of confinement for all births in the region covered by the Bristol flying squad from 1976–83. The per-

Table 1. The place of confinement for all births (expressed as a percentage of the total) in the region covered by the Bristol flying squad 1976–83

	1976	1977	1978	1979	1980	1981	1982	1983
Consultant obstetric units	80.5	84.9	87.0	88.4	88.9	90.7	91.8	92.4
GP units	18.3	14.1	12.0	10.8	10.2	8.6	7.4	6.6
Home	1.2	1.0	1.0	0.8	0.9	0.7	0.8	1.0
Total births	9470	9282	9894	10 303	10 707	10 245	10 124	10 028

centage of total births dealt with by consultant units in this period has risen from approximately 80% to 92%; this increase exactly matches the decrease in GP unit deliveries from approximately 18% to 6%. In fact, not only has the number of births in GP units fallen, but the actual number of units themselves has decreased from 15, in 1971 to 7, in 1984.

In contrast to the above figures, which are only available from 1974, the home confinement rate, as a percentage of total births, is available at irregular dates from 1950 to the present and this data is shown in Fig. 3.

Discussion

Over the period 1971–84, it can be seen from Fig. 1 that a greater than 20-fold reduction has occurred in the number of calls answered by the Bristol flying squad; in 1971, 84 calls were dealt with and by 1984 this figure had fallen to 3. In addition, by comparing Fig. 1 with Fig. 2 it can be seen that the proportion of calls made each year which require an anaesthetic to be given has also decreased.

In 1983, the last year for which comprehensive statistics are available, there were 10 028 births in the Bristol area, of which 9266 were delivered in consultant units, 662 were delivered in GP units and 100 were delivered at home (Table 1). Therefore, despite the trend to deliver in consultant units, there are still in excess of 750 births per year which take place without ready access to anaesthetic skills. It is likely that this number will be further reduced with more closures of GP units, because the large fall in home deliveries took place in the 1960s (Fig. 3) and the home delivery rate has been constant for the last 10 years or so at approximately 1% (Fig. 3 and Table 1). It is of course possible that the latter may rise if it again becomes fashionable to have home deliveries. Indeed, two recent articles[16,17] have urged a reassessment of the safety of both home and GP unit confinements and claim that it is a false assumption that consultant unit deliveries are safer.

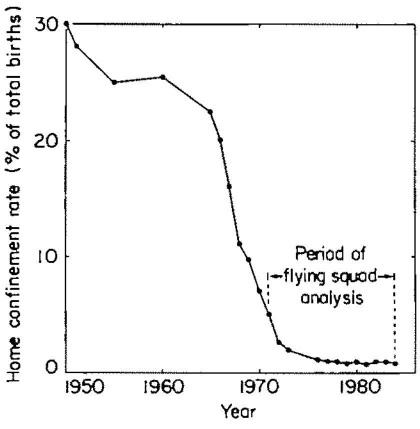

Fig. 3. The home confinement rate in the Bristol flying squad area.

The present low call out rate of the flying squad (Fig. 1) cannot be explained by the increase in consultant unit deliveries alone. The dramatic reduction in demand for flying squad services must reflect changes in obstetric practice and the increased awareness in the prediction of complications by obstetricians and general practitioners. The dangers of home confinements, and the need for more rigorous criteria before their acceptance, were in fact emphasised during the period of our survey in the Journal of the Royal College of General Practitioners.[9]

It is apparent that the retained placenta is the commonest obstetric complication which requires an anaesthetic to be given at the place of confinement. This complication comprises the reason for 84% of all the anaesthetic administrations over the 1971–84 period (Fig. 2). Throughout this time, of 172 cases occurring in GP units, only four were transferred to the base hospital prior to removal, whereas of 22 cases occurring in patients' homes, six were transferred with the placenta *in situ*. This difference of approach may reflect the anxiety felt by anaesthetists in hostile domestic surroundings as compared to the relative friendliness of the GP units, most of which have their own Boyle's machine, and electrocardiogram monitor, and provide a setting closer to that of a typical consultant obstetric unit.

The lack of adequate resuscitation in the management of retained placenta is a constant spectre running through the Reports on Confidential Enquiries into Maternal Deaths in England and Wales. There is comment in the 1955–57 report[10] on delays in starting transfusion and on the fact that 'death might have been avoidable by delaying manual removal until a supply of blood was available'. At that time, blood and infusion fluids were not as freely available as they are now, yet it is still claimed in the 1976–78 report[11] that 'too often blood loss has been underestimated ... Too little, too late seems to have been the fault in management'. There is, therefore, universal agreement that whenever disasters have occurred as a result of retained placenta, they are almost invariably associated with the undertransfusion of blood and replacement fluids. This may be because the problem only occurs in young, usually fit, women who apparently compensate well for a loss in circulating blood volume and the seriousness of the situation is not appreciated.

Given that resuscitation is adequate, the decision about transfer of the patient prior to anaesthesia is difficult. In both the 1970–72[12] and the 1973–75 report,[13] there is praise for the fact that no women suffering from postpartum haemorrhage were transferred to hospital with the placenta intact. It must, however, be remembered that the Reports on Confidential Enquiries into Maternal Deaths in England and Wales only investigate deaths. There is no record available of how many women were resuscitated properly, transferred safely with the placenta *in situ*, and then anaesthetised satisfactorily in the relative safety of a fully equipped obstetric unit. There may be many of these cases, since in some urban areas it has been the policy never to give an anaesthetic in domiciliary conditions, but always to transfer the patient to hospital, even if she cannot be adequately resuscitated.[14] A more moderate view of transferring patients appears in the 1967–69 report[15] where, although the authors initially caution particularly against transfer over long distances and recommend that 'it is safer for the flying squad to resuscitate the patient if she is shocked and remove the placenta in her home', they do concede that 'the risk of giving a general anaesthetic to the patient in her home must be recognised and it may be considered wiser to transfer the patient a short distance to hospital where anaesthetic skills and equipment are available'.

The decision whether or not to move a patient with the placenta *in situ* after whatever resuscitation, if any, is necessary, must be taken jointly by the anaesthetist and obstetrician; cardiovascular stability and a short distance would favour transfer, whereas cardiovascular instability and a long distance indicate removal at the place of confinement. Every anaesthetist is naturally anxious about giving an anaesthetic in domestic surroundings. No anaesthetist allocated to flying squad duty should, however, be so alarmed at this prospect, or so unfamiliar with the equipment provided for him, that fear of the unknown clouds his judgement and prevents him from giving an anaesthetic to those who really need it.

With this possibility in mind, it is salutary to examine the number of anaesthetics given in patients' homes and GP units over the period of the study; these data are shown in Table 2. There were 18 domestic anaesthetics administered, of which 16 were general anaesthetics for retained placenta, one was a spinal anaesthetic for a Kielland's rotation and the other was another general anaesthetic to investigate postpartum vaginal bleeding. It can be seen (Table 2) that, over the past 10 years, only four anaesthetics have been given in patients' homes. This must mean that the vast majority of junior anaesthetists have not only never given, but have never witnessed a domestic anaesthetic, despite being eligible to go out as the flying squad anaesthetist. Furthermore, possibly because of continued improvements in obstetric booking criteria, it can also be seen from Table 2 that no anaesthetic has been given in GP units for the past 2 years. This implies that the more recent junior anaesthetic staff may never have given any anaesthetic outside the hospital environment. It is probably fair to assume that this is not a feature peculiar to our area, since the pattern of change in obstetric practice is countrywide. Indeed, in 1930, the Belfast flying squad recorded that a 'virtually negligible number' of general anaesthetics is now required.[2]

Table 2. The number of anaesthetics administered to patients in GP units or in their own home

	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984
Number of anaesthetics given in GP units	41	43	33	30	22	12	4	4	3	4	2	6	0	0
Number of anaesthetics given in patient's homes	9	2	2	1	0	0	1	0	0	0	0	3	0	0

This change in demand for anaesthesia in the field raises three important questions. First, should there be an increased debate relating to the wisdom of, and guidelines for, moving of obstetric patients to anaesthetic services rather than *vice versa*; second, would the use of a general purpose mobile resuscitation unit be more cost effective than maintaining a dedicated obstetric flying squad; third, since the chance of ever having to employ anaesthetic skills in the domestic environment gradually diminishes, is it likely that complacency will increase in those who might be called upon to practise them? It should be remembered that despite the fall in demand for anaesthetic services, there are still 10 000 births per year in the Bristol area, of which over 750 occur without ready access to anaesthesia; sooner or later a bedroom anaesthetic is almost bound to be required.

It is opportune to draw to the attention of those anaesthetists who might be called out to an obstetric crisis, that it is their responsibility to be familiar with the equipment carried by the flying squad or local mobile resuscitation unit. It is essential that the anaesthetist does not meet his equipment for the first time in a crisis. The best way of preventing this is to use it, or identical equipment, from time to time during routine anaesthesia. For the anaesthetist to make the optimal judgement for a given patient requires him to be competent to administer an anaesthetic, if that is what is required. This, in turn, demands a familiarity and confidence with his equipment which is not gained if it never leaves its box.

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Anaesthesia, 1986, Volume 41, pages 726–730

HISTORICAL

Bedford Square

A connexion with mesmerism

C. A. FUGE

Summary

Nine Bedford Square has now been established as a Centre for Anaesthesia. It is a town house of considerable merit in the first square to have been planned on the London estate of the fifth Duke of Bedford. Built between 1775 and 1780, it is now the last complete Georgian square in Bloomsbury. This brief note on the history of Bedford Square shows that this part of London was prominent in nineteenth century medicine and, in particular, was involved in the early practice of mesmerism in this country. The place of mesmerism in the evolution of anaesthesia is restated and attention is drawn to the extraordinary coincidence that the new home that has been chosen for the Association of Anaesthetists of Great Britain and Ireland should be in an area which already has connexions with anaesthesia through mesmerism.

Key words

History.
Hypnosis.

The development of Bedford Square

It might be that Bedford Square (Fig. 1) would never have been built if John, the fourth Duke of Bedford, had not suffered from gout. It was as a result of this affliction that he made frequent visits to Bath to take the waters, during which he became a great admirer of that city's Georgian architecture. It was this admiration that inspired him to plan a square in the same style, to be laid out in one of the open fields of his Bloomsbury estate.[1] He did not survive long enough, as it happened, to see this development. After his death in 1771, the scheme was adopted by the fifth Duke of Bedford who commissioned the architects Thomas Leverton, William Scott and Robert Grews to design and build Bedford Square. It was the first square to be built on the Bedford estate[2] between 1775 and 1780, and it remains to this day the only complete Georgian square left in Bloomsbury.[3]

A fashionable residential area

With its private garden in the middle, the architecture of Bedford Square still shows the merit that attracted many famous people to live there during the nineteenth and early twentieth centuries. Indeed, one of the early residents was one of its own architects, Thomas Leverton. Apart from doctors and medical establishments (which are described separately below), there were politicians such as Lord Eldon (the Lord Chancellor at the time of the Corn Law riots in 1815) and H.H. Asquith, who lived there after his resignation as Prime Minister in 1916. In the early

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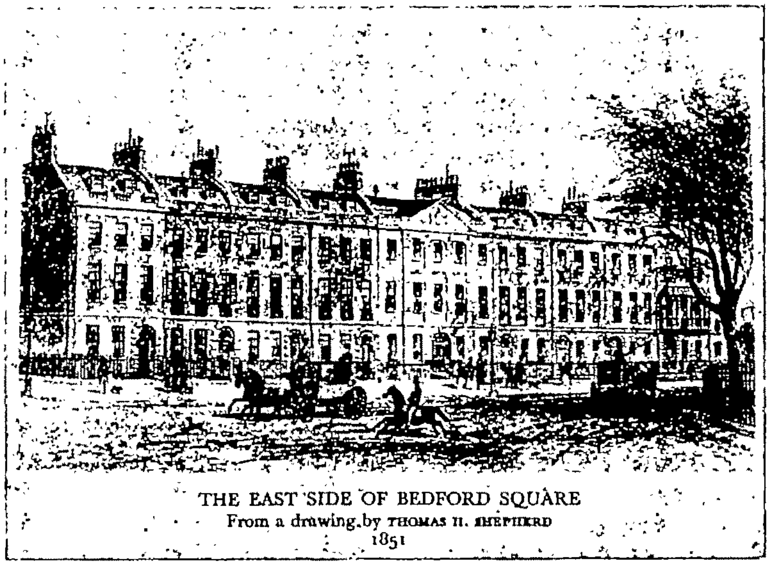
THE EAST SIDE OF BEDFORD SQUARE
From a drawing by THOMAS H. SHEPHERD
1851

Fig. 1. Bedford Square East Side, 1851. From a drawing by G.H. Shepherd (reproduced by kind permission of the Local History Library of the London Borough of Camden).

nineteenth century, there were scientists like Henry Cavendish and Sir Marc Isambard Brunel (father of Isambard Kingdom) and, in the first part of the twentieth century, the area had amongst its residents the actors Sir Seymour Hicks and Sir Johnston Forbes-Robertson, and the novelist Anthony Hope.

Bedford Square remained an exclusive and highly desirable residential address in London until the early part of this century. As late as 1893 the square was sealed off by gates and tradesmen were obliged to deliver goods by hand.[4] W.S. Gilbert, in one of his lesser-known short stories, which was originally published in the Temple Bar Magazine in 1880, referred to the contemporary appeal of such an address, when he had his day-dreaming bank clerk, Mr. Foggerty (a sort of nineteenth century Walter Mitty) '... desire only a brougham and pair to drive me home to a good house in Bedford Square'.[5]

Bedford Square today

In more recent times, Bedford Square has been largely nonresidential. Most of the houses are now offices, of which 14 (out of 53 addresses) belong to publishing houses, including Michael Joseph, William Heinemann, Hodder and Stoughton, Jonathan Cape, Edward Arnold and Frederick Warne. Other offices belong to a truly catholic selection of interests such as the Architectural Association, the Federation of Bakers, the Seafish Industries Authority and the U.S. Virgin Islands (Division of Tourism)! The only other building, apart from Nine Bedford Square to have any connexion with medicine is the annexe to the London School of Tropical Medicine.

Bedford Square and the history of medicine

The present day occupancy of Bedford Square is very much in contrast to that of the nineteenth century, when there was plenty of medical interest in the area. It was apparently well favoured by the medical profession since, in 1850, there were 11 doctors with registered addresses there, which compared well with the 14 registered in Harley Street at the same time.[6]

Number Nine itself was for many years in the first half of the nineteenth century a medical household—the home of Clement Hue, MD, FRCP, a distinguished, if somewhat troublesome Senior Physician of St Bartholomew's Hospital.[7] One of his sons, John Hue, FRCP, continued to live there after his father, while he held the appointment of Physician to the Seaman's Hospital, Greenwich. However, pre-eminent

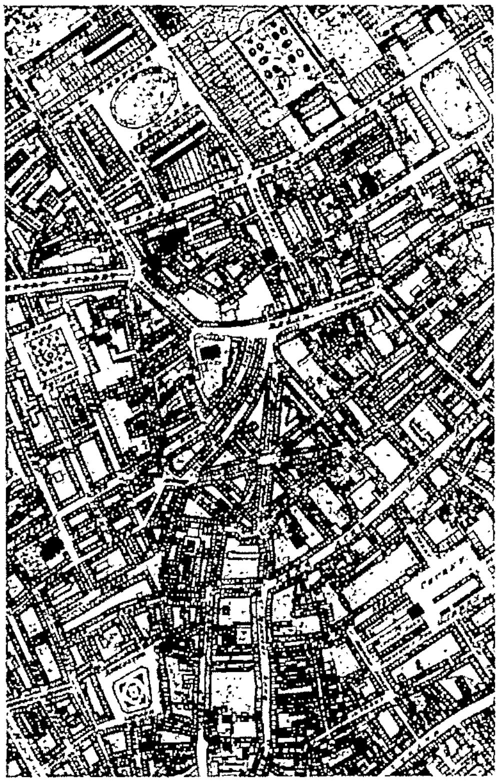

Fig. 2. Part of a map showing Bedford Square and Bedford Street. Horwood 1792 (reproduced by kind permission of the Guildhall Library, City of London).

amongst the medical fraternity in the mid-nineteenth century was Thomas Wakley, the outspoken founder editor of the *Lancet*, who lived at number 35. Across the square in Bedford Street was the Hunterian School of Medicine and, at number nine, from 1850–1852 was the London Mesmeric Infirmary.[8]

It was thought at one time that the latter establishment was in the house that is now the Association's headquarters,[9] but sadly for coincidence, it turned out not to be so. The address of the Infirmary was, in fact, 9, Bedford Street, Bedford Square, not 9, Bedford Square. The confusion may have arisen because Bedford Street, which connected the north-west corner of Bedford Square with Tottenham Court Road (Fig. 2) was renamed Bayley Street in 1878.[10] Even so, it can still be said that the London Mesmeric Infirmary was in the immediate neighbourhood of the new home of the Association of Anaesthetists.

The connexions with mesmerism

The connexions of this part of London with mesmerism (and the controversy which surrounded its introduction into this country) do not end here.

In 1878, at the same time that Bedford Square was being built, Franz Anton Mesmer, an aristocrat and a friend of Mozart, left Vienna to bring his new science of animal magnetism and hypnosis to Paris. In 1829, the French surgeon, Cloquet, amputated a breast painlessly under 'mesmeric sleep'. This was the first recorded instance of the use of mesmerism (as it was now called) for anaesthesia during surgery. Later that year, an Irishman named Chevenix, who had practised the art in Paris, visited London. He was invited to demonstrate his skills at St. Thomas's Hospital by one of the ablest physicians of the time, John Elliotson.

The Zoist

It was as a result of these demonstrations by Chevenix that Elliotson became an enthusiast for mesmerism, understandably one would think because, in 1829, this was the first real means of providing painless surgery. He and his followers even founded their own journal in 1843, called the *Zoist* (a Journal of Cerebral Physiology and Mesmerism and their Applications to Human Welfare). Over the next 12 years in which it was published, there were many papers and case reports in it which recorded the successful use of mesmerism.

Mesmerism as the inspiration for the search for a chemical anaesthetic

The popularity of the journal was some measure of the interest in mesmerism that was current, in spite of the contemporaneous discovery of the anaesthetic properties of nitrous oxide and ether. Indeed, one of Elliotson's disciples, a Scottish surgeon called James Esdaile, became a prominent figure in the movement supporting mesmerism, even though he himself had used ether successfully in 1846 and had acknowledged its virtues. John Elliotson acknowledged the virtues of etherisation, too, when he wrote in 1846: 'if this ... produces insensibility to pain in more instances than mesmerism, and quite as innocently as when mesmerism succeeds, it will be a blessing, and none will hail it more joyously than we mesmerists'. 'But', he went on to proclaim (about chemical anaesthesia) 'that to mesmerism and mesmerisers all this is really owing. The idea of providing insensibility for operations had, through mesmerism, laid such a hold on men that the trial of inhaling ether was made ...'[11]

James Esdaile continued to press this point. In 1853, the Congress of the United States of America offered $100 000 to the true discoverer of the anaesthetic properties of ether, which they described as the earliest anaesthetic. Esdaile responded to this by sending an open letter (which was published in the *Zoist*) entitled The Protest and Petition of James Esdaile MD to the Members of the American Congress, in which he drew attention to 'the simple and notorious fact ... that painless surgery by means of mesmerism, years before ether was heard of, was common in my hospitals'.[12]

The resignation of Dr Elliotson

John Elliotson continued to practise mesmerism enthusiastically even after he became the first Professor of Medicine at London University and on the staff of University College Hospital. He was an innovator and had a great reputation in London. Eminent Victorians such as Dickens (who lived in nearby Tavistock Square), Thackeray and Cruikshank were amongst those who were recorded as having attended his demonstrations.

But his reputation did not stop the vigorous opposition to him. The medical establishment, who disliked his controversial methods, were outspoken in their criticism. Prominent amongst his opponents was Robert Liston who was an active adversary in the Medical Committee of University College Hospital. So too was Thomas Wakley who waged an acrimonious and relentless editorial campaign in the *Lancet* against Elliotson and what he called the 'Mesmeric Humbug'.[13] It was in Wakley's house in Bedford Square that the debacle over the use of mesmerism to treat the O'Key sisters took place[14]—the affair which finally forced Elliotson to resign from the staff of University College Hospital.[15]

The mesmeric infirmaries

As a consequence of all this, the mesmerists eventually decided to found their own institutions in which to practise their art. In spite of the proximity of Thomas Wakley's house, the London Mesmeric Infirmary was established in Bedford Street in 1850. Others were set up in Bristol, Exeter and Dublin, but none of them lasted long. In fact, the London Infirmary moved twice, in 1853 to Fitzroy Square and in 1854 to Weymouth Street.[15]

Mesmerism and the evolution of anaesthesia

Most historians would agree with John Elliotson and James Esdaile and, like them, hold that mesmerism has a rightful place in the evolution of anaesthesia, and that at least some credit should go to the mesmerists for the inspiration to search for a chemical anaesthetic.[17] Even Liston appeared to give some credence to the view that mesmerism had played a part, when he made his famous remark about ether. 'This Yankee dodge beats mesmerism hollow!'—even if this was a backhanded acknowledgment.

It seems appropriate that the new centre for anaesthesia should be established in a part of London which has these historical connexions with the evolution of anaesthesia, and that anaesthetists should appreciate this. In his editorial last year, Professor Rosen was quite right to appeal to anaesthetists for a sense of history and to challenge Henry Ford's well-known opinion of it.[18] The view of Sir Winston Churchill[19] is surely much to be preferred.

'The longer you can look back, the further you can look forward.'

Acknowledgments

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Anaesthesia, 1986, Volume 41, pages 731–733

CASE REPORT

Repeated deep accidental hypothermia

A comparison of active or passive treatment in one patient

N. E. DRENCK AND H. v. STAFFELDT

Summary

Deep accidental hypothermia after self-poisoning with drugs occurred twice in the same patient within 25 days. Initial rectal temperatures were 22.0°C and 23.3°C, respectively; the clinical conditions were otherwise identical. In the first instance, active rewarming by means of peritoneal irrigation was performed, while spontaneous rewarming was allowed on the second occasion. Normothermia was attained within 24 hours in both cases, and the patient was discharged in her habitual state of well-being.

The course of these nearly identical cases illustrates the possibility of a passive treatment for deep hypothermia.

Key words

Hypothermia; intensive therapy.

Deep hypothermia is characterised by a body core temperature (Tc) of less than 30°C, decreased consciousness, severely reduced ventilation, shock and absence of muscle activity with loss of reflexes. Complications such as cardiac dysrhythmias, hypokalaemia and acidosis occur. The condition is potentially life-threatening, and even with intensive therapy, the mortality rate is 27 percent.[1]

Treatment involves re-establishment and support of vital functions and thermal insulation of the patient, so that loss of endogenous heat is minimised. Such treatment is referred to as passive. There are several alternatives for active therapy.[2] of which one is peritoneal irrigation with heated fluids.[3] Because of the lack of controlled studies to establish the possible advantages of active treatment, rational treatment of hypothermia is still under debate.[4]

The only proof that passive therapy has been inadequate is the failure of Tc to increase. In spite of this involved, active, therapy is often initiated without a demonstration of an increase in Tc, even though any active therapy holds a possibility of severe complications. Active or passive rewarming can lead to the same successful outcome within equivalent periods of time. This is illustrated by two instances of hypothermia that occurred to the same person.

Case history

A 65-year-old, physically healthy woman with a tendency to depression, was admitted to the same hospital ward twice within a 25-day interval and under identical circumstances, with deep accidental hypothermia.

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First admission

The patient was found in her home after taking an overdose of levomepromazine. Upon arrival in the hospital, blood-pressure (BP) and pulse were unmeasurable and respiratory rate was 2/minute. Electrocardiogram (ECG) showed nodal bradycardia, with a heart rate of 40/minute and with an obvious J-wave (Osborne-wave). Rectal temperature measured with a mercury thermometer was 22.0°C. The patient was comatose, without muscle activity or reflexes. Her trachea was intubated and her lungs ventilated, initially with humidified 100 percent oxygen heated to 37°C. Her body was covered with blankets and the ambient temperature was held at 25°C. The femoral artery and vein were cannulated and 1 mg adrenaline and 1 mg atropine were given intravenously. The heart rate rose to 60/minute and mean arterial pressure to 40 mmHg.

Sixty minutes after arrival, peritoneal irrigation was begun, using isotonic dialysis fluid heated to 37°C at approximately 4000 ml/hour. During the following day, 3800 ml of heated (37°C) fluids were infused intravenously. The rectal temperature and the skin temperature of the right great toe were recorded continuously (Fig. 1). Peritoneal irrigation was concluded after 17 hours, when the rectal temperature was 36°C and ventilation was adequate.

During rewarming, the cardiovascular state was quickly restored to normal and remained stable. No cardiac dysrhythmias which required treatment were observed. The patient was awake and in her habitual state of wellbeing after 36 hours.

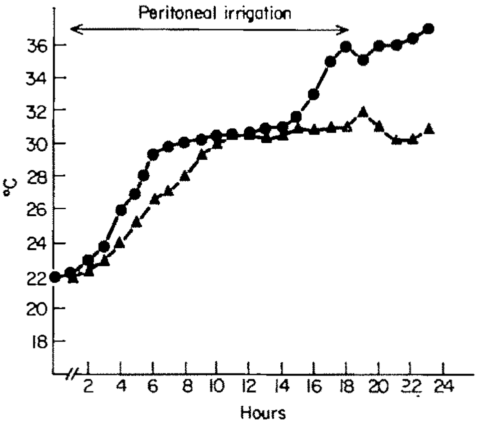

Fig. 1. Course of rectal temperature and skin temperature of right great toe, during the first admission. The duration of peritoneal irrigation is marked by an arrow. ●, Rectal temperature; ▲, skin temperature.

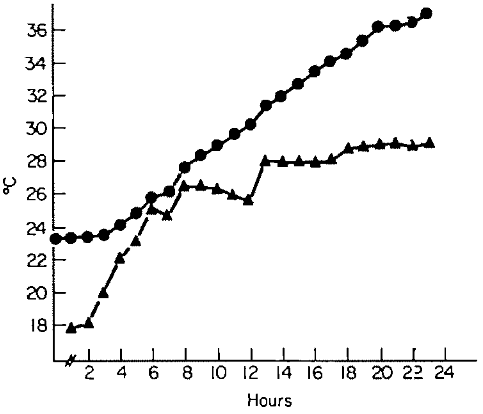

Fig. 2. Course of temperatures during the second admission. ●, Rectal temperature; ▲, skin temperature.

Second admission

This occurred 25 days after the first incident. The patient was found in her home after poisoning with an unknown drug. Her condition upon arrival at the hospital was identical with that of the first hospitalisation, although the rectal temperature was 23.3°C on this occasion. A course of treatment was started which differed from that of the first admission only with regard to peritoneal irrigation, because the necessary resources were not immediately at hand. Despite this, the rise in Tc which developed over the following hours was considered satisfactory and more active therapy was deemed unnecessary (Fig. 2). The clinical course was otherwise as described for the first admission.

During both admissions there was initial hypokalaemia, which required correction by intravenous infusion, and no hypokalaemia occurred during rewarming. Severe acidosis (pH 6.98) and base excess (−16 mmol/litre) was observed during the second admission; this was corrected in part by infusion of 100 mmol sodium bicarbonate, and then allowed to revert to normal spontaneously within the following 10 hours.

Discussion

On both admissions of this patient we found characteristic, well documented, slowly-developing, deep accidental hypothermia. The clinical pictures in both cases were similar and the close temporal relation between the two results in what must be a unique controlled, clinical experiment.

The figures demonstrate that no after-drop in rectal temperature occurred and the most marked increase of rectal temperature was at the beginning of treatment, when peritoneal irrigation was performed. The critical temperature of 28°C below which there is usually an associated increased risk of fatal cardiac dysrhythmia[5] was attained 3 hours earlier with active rather than with passive treatment.

It appears that the temperature gradient between body core and surface is least when peritoneal irrigation is performed, thus reducing the risk of an after-drop in Tc. Subsequent testing on another hypothermic patient suggests that despite possible local warming of the electrode placed just inside the rectum, there was less than 1°C difference from core temperature measured at the tympanic membrane. It is notable that normothermia was reached in both instances after 23 hours, regardless of therapeutic method. The rate of increase for Tc with peritoneal irrigation could have been increased by either raising the fluid temperature or by raising the flow; neither of these were done because the clinical progression was considered satisfactory. No hypokalaemia occurred during any of the rewarming periods. The role of the potassium content of the dialysis fluid is not known.[3]

The only obvious difference between the cases is the absence of acidosis at the first admission; we have found no plausible explanation for this. With the second admission, causes of acidosis such as poisoning with ethanol, barbiturates or acetylsalicylic acid were excluded on the basis of blood analysis. The difference in the core–skin temperature gradients in the two admissions may be accounted for by the known ingestion of a potent alpha-adrenergic blocking agent (levomepromazine) on the first occasion, and the small gradient then might result from peripheral vasodilatation. The larger gradient in the second admission may result from the fact that no alpha-adrenergic blocking agent was ingested.

The clinical courses of these two cases of hypothermia demonstrate that the same therapeutic result may be attained either by active or passive therapy. In our opinion, however, active therapy by means of peritoneal irrigation gives a higher degree of security. Ideally, the treatment of each case of slowly developing, deep accidental hypothermia should be carried out after an evaluation of the patient's heat loss. As a consequence, our present policy of treatment involves active rewarming only when Tc fails to rise within a few hours, provided that circulation is not impaired.

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Anaesthesia, 1986, Volume 41, pages 734–738

CASE REPORT

Anaesthetic management of Takayasu's arteritis

J. R. THORBURN AND M. F. M. JAMES

Summary

A case of type IV Takayasu's arteritis in whom a renal autotransplant was performed is presented. Extensive cardiovascular measurements were made, which enabled the assessment of vascular responsiveness to various anaesthetic manipulations. The management of the condition is discussed and certain recommendations made in light of the experience gained.

Key words

Arteries; occlusive panarteritis, Takayasu's arteritis.

Takayasu's arteritis is a chronic occlusive panarteritis, potentially affecting all large and medium calibre arteries in the body, and is commonest in young females.[1] It is a progressive disease that is frequently fatal. It has been classified on the basis of the distribution of affected vessels.[2,3] In type I, the disease affects the aortic arch and its branches; in type II, the descending thoracic and abdominal aorta is involved without involvement of the arch; type III displays a mixture of the features of both types I and II. Following description of the involvement of the pulmonary arterial system,[4] the classification has been extended to include a fourth type,[3] which may involve any of the features of the first three types and, in addition, involves the pulmonary artery. This report describes the anaesthetic and immediate postoperative management of a patient with type IV disease.

Case history

The patient was a 20-year-old female who originally presented to this hospital with severe hypertension which was thought to be due to bilateral renal artery stenosis demonstrated on aortography. There was also involvement of the abdominal aorta, coeliac axis and superior mesenteric artery. The diagnosis of Takayasu's arteritis (TA) was made at this time. Renal function and plasma renin levels were normal on this occasion. Renal scan showed adequate function bilaterally. Her hypertension was adequately controlled with captopril, alpha methyldopa, frusemide and hydralazine, with oral potassium supplementation. Relevant previous history included an attack of anterior poliomyelitis 5 years earlier, which left a residual weakness in both legs, but the patient remained fully mobile.

She was re-admitted, complaining of decreased exercise tolerance, orthopnoea, paroxysmal nocturnal dyspnoea and pedal oedema 11 months later. She was found to be in cardiac failure and her arterial blood pressure was 190/110 mmHg. She responded to increased dosages of all

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her drugs. Once her cardiac failure had been controlled, a flush aortogram was performed. This showed progression of her disease in all previously affected arteries, with complete occlusion of both renal arteries. Renal perfusion was maintained by an extensive collateral network. The abdominal aorta was narrowed and irregular, but the aortic arch and its branches were normal. These features were reported as being consistent with Takayasu's arteries type II. Dimercapto succinic acid (DMSA) scan showed a renal tubular mass of 62% of normal on the right, and 38% on the left. The creatinine clearance was 46 ml/minute. It was decided to perform a left renal autotransplant in an effort to preserve renal mass.

Pre-operative assessment

The patient was a well looking young woman. Her heart rate was 94 beats/minute, her arterial blood pressure 150/100 mmHg. Right-sided failure was shown by a markedly elevated jugular venous pressure, a right-sided gallop, a loud pulmonary second sound, an enlarged liver and ankle oedema. On this basis, pulmonary involvement was presumed and she was reclassified as a type IV. She was mildly breathless and tachypnoeic, but her chest sounded clear. On investigation she was found to have an ESR of 36 mm/hour and a blood urea of 6.8 mmol/litre (Reference range: 3.5–6.5 mmol/litre); all other values were within normal limits. Pulmonary function testing showed a marked restrictive pattern and mild hypoxia breathing air. ($P\text{a}O_2$ 8.5 kPa at barometric pressure of 80 kPa). ECG showed right-sided predominance, but no evidence of ischaemia. Echocardiography reported a myopathic heart with poor contractility. Chest radiography was noncontributory.

Anaesthetic technique

Diazepam 10 mg orally was given as premedication, and all antihypertensive medications continued up till the time of surgery. A 7FG right internal jugular catheter was inserted under local anaesthesia before induction and a flow directed pulmonary artery catheter positioned. An estimation of cardiac output (CO) was obtained by thermodilution and cardiac index (CI) calculated. Readings were made of right atrial pressure (RAP), pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP). At this stage, blood pressure was measured indirectly and systemic and pulmonary vascular resistances (SVR and PVR) calculated. Following pre-oxygenation, anaesthesia was induced with fentanyl 0.25 mg and etomidate 14 mg, the patient was paralysed with pancuronium 6 mg and the trachea intubated following a further 2 mg of etomidate and 60 mg lignocaine intravenously. The lungs were ventilated with 50% oxygen in nitrous oxide and halothane 0.75–1%. Analgesia was maintained with incremental doses totalling 0.2 mg fentanyl and 35 mg papaveretum. Ulnar arterial flow was judged to be insufficient to justify radial artery cannulation, and a cut down cannulation was therefore performed on the right ulnar artery. Once arterial blood gas analysis was available, ventilation was adjusted to maintain normocarbia.

There was a small decrease in blood pressure accompanied after induction by an unacceptable decrease in CI. In view of this and the high SVR, halothane was temporarily discontinued and an infusion of sodium nitroprusside started at a rate of 0.6 μg/kg/minute. This produced a fall in SVR from 29.3 mmHg/(litres/minute) to 23.0 mmHg/(litres/minute), with a concomitant rise in CI. Increasing the nitroprusside infusion rate to 1.2 μg/kg/minute further reduced SVR to 16.3 mmHg/(litres/minute) and produced a further rise in CI (Table 1). Halothane was reintroduced and anaesthesia continued uneventfully.

With a view to simplifying postoperative blood pressure control, a total of 15 mg of dihydralazine was introduced in divided doses and nitroprusside slowly withdrawn; thus, similar levels of systemic vascular resistance were maintained. The patient was electively ventilated postoperatively and analgesia provided with intravenous papaveretum by titration. Further increments of dihydralazine were given as required to control blood pressure. The following morning, the control of pain and blood pressure were considered to be suboptimal, and this precluded discontinuation of ventilation. Accordingly, an epidural catheter was inserted at T_{9-10} interspace using the lateral approach. Eight ml 0.5% bupivacaine plain was injected with the usual precautions and good pain relief was achieved. This produced a considerable fall in both SVR and PVR. Epidural analgesia was continued with

Table 1. Cardiovascular changes connected with various events during the peri-operative period

Event	SBP	BP	PAP	RAP	PCWP	CI	SVR	PVR
Pre-induction	170	130	43	11	7	2.7	26.4	8.0
Halothane, nitrous oxide anaesthesia	139	93	38	5	14	1.8	29.3	8.0
Nitroprusside 0.6 ug/kg/minute	143	100	41	1	16	2.6	22.8	5.8
Nitroprusside 1.2 ug/kg/minute	170	106	40	16	17	3.3	16.3	4.1
Nitroprusside 0.2 ug/kg/minute + dihydralazine 5 mg	134	86	34	7	5	3.6	13.1	4.7
Dihydralazine 15 mg	140	87	36	11	11	3.6	12.8	4.1
1st Post-op Day								
Analgesia alone	180	120	40	6	14	3.2	21.4	4.9
Dihydralazine 12.5 mg	163	109	47	6	11	3.7	16.8	5.7
Pre-epidural	169	117	40	5	4	3.3	20.3	6.5
Postepidural	138	89	34	5	3	4.0	12.6	4.6

SBP, systolic arterial blood pressure (mmHg); BP, mean arterial blood pressure (mmHg); PAP, mean pulmonary arterial pressure (mmHg); RAP, right atrial pressure (mmHg); PCWP, pulmonary capillary wedge pressure (mmHg); CI, cardiac index (litres/sq m); SVR, systemic vascular resistance (mmHg/(litres/minute)); PVR, pulmonary vascular resistance (mmHg (litres/minute)).

bupivacaine 0.5% and a single dose of 3 mg epidural morphine which provided excellent analgesia and blood pressure control. This facilitated rapid weaning from the ventilator and tracheal extubation. All cardiovascular changes in the peri-operative period are summarised in Table 1.

The postoperative course was complicated by a right basal pneumonia, and at 10 days by a small pulmonary embolus, but the patient eventually made a good recovery with a return to pre-operative renal function status.

Discussion

The first description of nonspecific arteritis was made by Savory and Kussmaul[5] in 1856 and in 1908 Takayasu[6] noted ocular changes in the retinal vessels of a young woman. In discussion of Takayasu's presentation, similar retinal changes were described by Onishi and Kagoshima[7] in two cases with absent pulses in the arms. Shimizu and Sano in 1948 detailed the findings in this disorder,[8,9] which was named Takayasu's arteritis (TA) in 1954 by Caccamise and Akuda.[10]

Pulse deficit is the commonest presentation and hypertension and cardiac failure occur frequently. The heart failure usually follows systemic or pulmonary hypertension.[3,11] Systemic hypertension is generally moderate and usually responds to medical treatment. Myocardial damage is secondary to heart failure and is not a feature of the disease itself. Coronary involvement is a rare complication.[11] The manifestations of the disease are determined by the distribution of the vessel involvement and thus typing has important implications for management. Approximately 45% of patients have TA with pulmonary involvement (type IV),[3,11] and 50–60% of these have right heart strain.[3,11,12] Renal involvement has been found in 63% of cases, but organ perfusion is often preserved by well established collaterals.[11]

In assessing a patient with TA presenting for surgery it is important that the type, and hence the distribution of the arteritis, is established and the degree of organ involvement ascertained. Particular attention must be paid to cardiac, respiratory and renal function. Since hypertension and cardiac failure usually respond well to treatment, every effort must be made to ensure optimal preoperative cardiovascular function.

Previous reports of the anaesthetic management of this condition have emphasised the importance and difficulty of adequate cardiovascular monitoring.[13–15] We were fortunate in this case that the distribution of the disease allowed for good recordings of upper limb arterial blood pressure. An arterial line was considered mandatory to ensure adequate pressure monitoring, as excessive disturbances of blood pressure in either direction could have serious consequences for regional organ perfusion.[15] However, the pressure measured in one area may not reflect organ perfusion in another. It may well be argued that we should also have monitored the blood pressure in the leg, in order to have some measure of overall perfusion, although in this case it was possible to estimate renal arterial filling by direct inspection. The placement of an arterial line was also considered necessary to provide access for repeated blood gas analysis in view of the pulmonary disease. The decision to insert the arterial cannula under direct vision was made in order to minimise the risks of abortive attempts in already compromised vessels.

Our experience in this case demonstrated that isolated blood pressure monitoring may not accurately reflect haemodynamic status and we consider that a Swan-Ganz catheter should be inserted in all cases. This is supported by Lupi *et al.*[3] who advocated routine evaluation of the pulmonary circulation in this condition, and by Warner and his colleagues who also felt that this procedure was warranted.[14] As predicted by their reports, no difficulty was experienced in placing the pulmonary artery catheter. The insertion of a pulmonary artery catheter prior to induction permits detailed assessment of myocardial function as well as measurement of the calculated SVR and PVR. Symptoms of pulmonary arterial involvement may be absent, so this may be the only way of diagnosing type IV TA. In extensive forms of the disease, where measurement of the peripheral blood pressure is impossible, this may provide the only means of haemodynamic monitoring.

Our cardiovascular findings were interesting. The fall in cardiac index following induction suggested that the myocardium was particularly sensitive to negative inotropic agents. The degree of vascular responsiveness to vasodilator agents resulted in a satisfactory improvement in myocardial function. Vasodilatation might be anticipated in such cases, as Nakao *et al.* reported that vasodilators provided symptomatic relief in some of their patients, but the degree was not quantified.[16] The ability of the heart to respond to afterload reduction suggests that the degree of cardiomyopathy was less than that predicted from the echocardiograph.

Pulmonary function was well maintained throughout the procedure and gas exchange presented no problems. However, high ventilator pressures were required, as anticipated from the restrictive nature of her pulmonary disease. Although the systemic vascular resistance was readily restored to normal levels, pulmonary vascular resistance, while responding well, always remained above the normal range. The very high pulmonary artery pressures present in this patient are unusual, and are found in only a few cases. More commonly, the pulmonary hypertension is of a moderate degree, and pulmonary symptoms are rare or absent, although 72% are reported to have detectable clinical, ECG and X ray abnormalities.[3] The marked restrictive lung disease and subsequent postoperative pulmonary complications were possibly a reflection of the severity of the pulmonary disease in this patient and need not necessarily be anticipated in other cases of type IV TA.

There are no other reports of the use of epidural anaesthesia in this condition. The decrease in SVR and increase in cardiac index which followed epidural anaesthesia compared favourably with that obtained from the use of vasodilator drugs. Surprisingly, epidural blockade reduced both SVR and PVR. Presumably, this was because the blockade extended sufficiently high to block thoracic sympathetic outflow. Although we did not use epidural blockade intra-operatively in this case, the beneficial effects on vascular resistance and cardiac performance demonstrated in the postoperative period, suggest this technique would have been a useful adjunct to the intra-operative management. Some form of vasodilatation is likely to be needed in cases of this type, both for the control of blood pressure and to reduce the afterload to assist the compromised ventricle. The use of epidural blockade as part of the anaesthetic may have achieved this without recourse to potent intravenous vasodilator agents, perhaps with the advantage that vasodilatation would be limited to the affected areas. In addition, the need for myocardially depressant anaesthetic agents could have been reduced. Our findings in this case indicate that epidural blockade should be considered in cases of this type.

Acknowledgments

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Anaesthesia, 1986, Volume 41, pages 739–741

CASE REPORT

Suxamethonium-induced hyperkalaemia following cold injury

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Summary

Within the space of 9 days, a 4-month-old baby requiring cardiac surgery was exposed to two periods of hypothermic circulatory arrest for surgery, and prolonged surface cooling postoperatively. At the end of this period, the administration of suxamethonium was associated with a marked rise in serum potassium.

Key words

Neuromuscular relaxants; suxamethonium.
Ions; potassium.

The occurrence of hyperkalaemia following the administration of suxamethonium is well documented in burns patients.[1] A case of an infant who developed hyperkalaemia following hypothermia is reported.

Case history

A 4-month-old, cyanosed, male infant was readmitted for further treatment of pulmonary atresia and triscuspid valve disease. He had undergone as a term neonate at one day of age cardiac catheterisation and balloon atrial septostomy followed by pulmonary valvotomy and ligation of a patent ductus arteriosus. Six hours later he was again operated on for the creation of a modified Blalock-Taussig shunt. At 4 months he weighed 3.9 kg, and, after cardiac catheterisation, it was decided to repair his right ventricular outflow tract.

The infant was prepared for surgery in the standard fashion employed at the Wessex Cardiothoracic Centre.[2] Following induction of anaesthesia, surface cooling with ice was used to reduce core temperature to 28°C. Once cardiopulmonary bypass was established, core temperature was reduced to 13°C and the circulation arrested for 36 minutes while the definitive surgery was performed. During the procedure, considerable stenosis of the triscuspid valve with fusion of the valve leaflets was evident, and these were therefore divided. He was then rewarmed to 36°C before withdrawal of cardiopulmonary bypass. Postoperatively, the infant was hypoxic, with right ventricular failure, and received dopamine and sodium nitroprusside to maintain peripheral circulation. After 36 hours, the child's condition was deteriorating and he was therefore cooled to a temperature of 33°C in the hope that this would allow time for right ventricular function to improve.

Over the next 4 days, the clinical state of the child remained poor and his temperature was maintained at 33°C. In view of the intractable right ventricular failure, repair of his tricuspid valve was undertaken. This was per-

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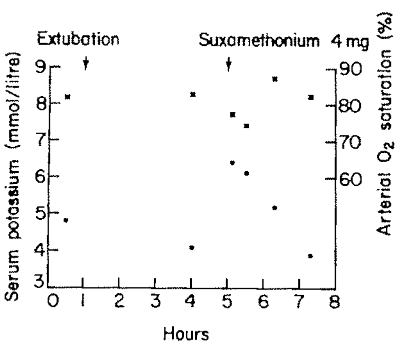

Fig. 1. Arterial oxygen saturation and serum pottassium, before and after administration of 4 mg suxamethonium. ●, Serum potassium; ×, arterial O_2 saturation.

formed as before under hypothermic circulatory arrest at 13°C for 31 minutes. Following this last operation, dopamine and sodium nitroprusside were continued, and the child's temperature was kept at 33°C. Over the next 3 days his condition slowly improved, and on the fourth day he was rewarmed; the amount of pharmacological support needed was minimal.

The nursing staff had noticed that following the last operation the subcutaneous tissues of the child had a 'woody' feel to them, and this persisted when the child was rewarmed. Five days postoperatively, intermittent positive pressure ventilation (IPPV) was discontinued. On the sixth day, his trachea was extubated. Over the space of 4 hours, despite a good colour and an adequate arterial oxygen saturation (Fig. 1). he rapidly tired and it was therefore decided to reinstitute IPPV. In order to facilitate intubation suxamethonium 4 mg was administered intravenously after pre-oxygenation. During intubation the pulse rate fell from 140 to 40 beats/minute, rising to 120 when atropine 0.05 mg was given. The ECG showed high peaked T-waves. Serum potassium measured by flame photometer at this time was 6.4 mmol/litre. Figure 1 shows the time course of changes in serum potassium before and after suxamethonium. The infant's trachea was extubated without mishap 2 days later, and normal turgor of the subcutaneous tissues returned over the next week without development of any ischaemic zones.

Discussion

Dangerous rises in serum potassium levels following suxamethonium administration are well documented in patients with burns,[1] neuromuscular disorders,[3] muscle trauma,[4] tetanus[5] and uraemia.[6] Serum potassium generally rises to a peak over 3–5 minutes, before returning to normal over the space of the next hour. In burns patients, sensitivity to suxamethonium appears about 5 days after injury and continues for 2–3 months.[7] In these patients, sensitivity may be due to muscle membrane damage,[3] or may be caused by increased chemical sensitivity related to disuse atrophy.[8]

In our patient, thermal injury was suspected because of the abnormal feel of the subcutaneous tissues after two short periods of profound hypothermic circulatory arrest at 13°C and 8 days of mild hypothermia at 33°C. Six days elapsed between detection of the injury and administration of suxamethonium. However, prior to the use of suxamethonium, it was not thought that this situation could be equated with one of burns trauma. Serum potassium rose by 2.3 mmol/litre as compared with a rise of 0.45 mmol/litre in normal children.[9] Our experience would suggest that consideration should be given to the use of suxamethonium, not only in patients who have recently undergone cardiac surgery with hypothermic circulatory arrest, but also in patients who have suffered cold injury from exposure or immersion.

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Anaesthesia, 1986, Volume 41, pages 742–744

APPARATUS

Survey of alarms in an intensive therapy unit*

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Summary

The origin and frequency of alarm soundings in a general purpose intensive therapy unit were recorded by the nursing staff for 3 weeks. Only eight out of a total of 1455 soundings indicated potentially life threatening problems. There were many false alarms from the monitoring system and the infusion rate pump. The overall frequency of soundings varied little by day or night. There is a need for a graded system of alarms to reflect the priority of the disturbance detected.

Key words

Equipment; alarms.

As the variety of equipment used in the intensive therapy unit (ITU) has increased, so has the incidence of alarms, posing difficulties for all staff working in ITU.[1] This study was carried out to provide data on the frequency and origins of alarm calls in a general purpose ITU.

Methods

The nursing staff recorded all alarm calls in the ITU during a 3-week period. They noted equipment source, why the alarm sounded and whether it was silenced. They were particularly asked to state whether the alarm call had drawn their attention to a life threatening incident.

A total of 26 patients, 20 adults aged 19–79 years (mean 52 years), 6 children aged 8 months–11 years (mean 3.7 years), mean stay 3.2 days, were admitted during the 3 week study period. The mean bed occupancy was 4.48 patients.

Results

A total of 1455 alarms were recorded; their origins are shown in Fig. 1. Only eight alarms indicated potentially serious problems, one ventilator disconnexion and seven serious dysrhythmias requiring treatment.

Ventilator alarms (Table 1) were mostly triggered during suction or physiotherapy, despite a delay time of 15 seconds for the Servo 900C and 12 seconds for the Cape 2000. A fault on one Cape 2000 frequently caused the low pressure alarm to sound. The alarms on these ventilators are self-terminating once the problem has been corrected. Only 25% of the monitor alarms indicated a dysrhythmia, while 75% were false alarms, triggered by the removal of the ECG leads (Table 2). The infusion devices sounded an alarm to indicate a completed infusion or blockage. The causes of the alarms are shown in Table

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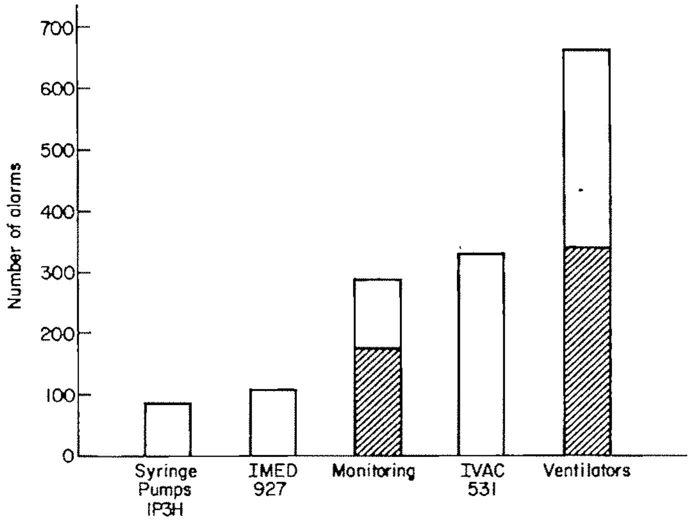

Fig. 1. The source of 1455 alarms and the proportion silenced by the nursing staff. □, Total number of alarms; (■), silenced alarms.

3. The majority of the IVAC 531 alarms were caused either by incorrect alignment or for no traceable reason.

The distribution of alarms between shifts and throughout the study was broadly similar but individual patient alarms showed a wide variation (Table 4).

Discussion

Although there was little variation in the overall frequency of alarm soundings by day or night throughout the 3 weeks of the study, the number of alarms per patient varied considerably. This reflects both the level of dependency of each patient and the ability of the nursing staff to anticipate alarm sounding; indeed, 'silent' shifts were recorded with pride.

All the alarms could only be reset once the fault had been corrected. The IVAC 531 pumps and Vickers IP3H syringe pumps must be switched off to silence the alarm. The warning devices on the ventilators, monitoring systems and IMED 927 volumetric infusion pumps can all be muted, but continue to display a visual warning. However, if an alarm signal is silenced without correction of the original fault, the possibility of harm to the patient still remains.

The unreliability of the ECG monitoring is disturbing for an 'immediate' alarm and the electrode connexions should be improved. The

Table 1. Ventilator alarms

	Number	Silenced (%)
Suction	204	62
Physiotherapy	152	57
Restless patient	112	14
Low pressure/minute volume	101	47.5
Alteration to breathing system	55	51
Humidifier	16	100
Other causes	21	66

Table 2. Monitor alarms

	Number	Silenced (%)
Leads removed by		
nursing care	39	38
patient movement	175	64
Tachycardia HR > 160/minute	44	79
Bradycardia HR < 60/minute	26	46

Table 3. Infusion device alarms

Equipment	Number
Vickers IP3H Syringe Pumps	
blockage	22
infusion completed	54
incorrect assembly	2
IMED 927	
blockage	46
infusion completed	60
IVAC 531	
blockage	30
infusion completed	76
incorrect alignment	97
no traceable reason	114
priming	9

Table 4. Alarms per shift

	Morning (5 hours)	Afternoon (9 hours)	Night (10 hours)
Total	338	438	595
Average hourly rate	3.2	2.3	2.8
Number per patient (range)	0–16	0–26	0–38

drip rate pumps performed as well as the other infusion devices, but generated many unnecessary alarms. A high false alarm rate may distract the attendant's attention from an important alarm, as well as making unnecessary noise close to the patient.

In a recent comprehensive review on warning devices, Kerr[2] suggests five ways in which alarm sounds might be allocated, but stresses that 'there is currently insufficient evidence to provide overwhelming support for any particular allocation system'. The majority of alarms in this study signalled minor malfunctions, rather than events which threatened patient safety. This result illustrates the need for rationalising alarm systems and it is suggested that the 'risk and response approach' would best safeguard patients admitted to this ITU.

Acknowledgments

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Anaesthesia, 1986, Volume 41, pages 745–748

Forum

Cardiac dysrhythmias during oral surgery. Comparison of hyoscine and droperidol premedication

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Summary

The incidence of cardiac dysrhythmias during inpatient dental anaesthesia under halothane was studied following either hyoscine or droperidol as a supplement to papaveretum for premedication. Forty-three percent of patients given hyoscine exhibited cardiac dysrhythmias compared to 23 percent of the group given droperidol ($p = 0.03$). The incidence of dysrhythmias bore no relationship to the age, sex or weight of the patient, nor to the end tidal carbon dioxide tension.

Key words

Complications; dysrhythmia.
Premedication; droperidol, hyoscine.

Anaesthesia for oral surgery continues to be associated with a high incidence of cardiac dysrhythmias (Table 1). The aetiology of these abnormal rhythms is obscure,[1,2,3] but it is known that stimulation of the trigeminal nerve increases circulating catecholamine levels,[1] in addition to the increase in catecholamines exhibited by dental patients as a result of anxiety.[4] Halothane slows conduction to differing degrees throughout the heart, depresses myocardial contractility[5] and sensitises the myocardium to the dysrhythmogenic effects of circulating catecholamines.[6] Anticholinergic drugs used for premedication depress vagal tone and reduce the refractory period of the atrioventricular node, so that in the presence of high catecholamine levels, the combination of halothane and hyoscine may increase the likelihood of re-entry dysrhythmias arising from ectopic foci in the ventricle.[7,8] Hypercarbia is traditionally thought to potentiate halothane-induced dysrhythmias,[2,3,9] but there is dispute over the clinical significance of this.[1,10,11]

Table 1. Reported incidence of cardiac dysrhythmias during dental surgery in adult patients anaesthetised with halothane

Date	Authors	Incidence
1966	Kaufman[25]	50%
1968	Rollason and Dundas[11]	18%
	Tuohy[2]	27%
1971	Alexander[28]	23%
1972	Thurlow[16]	19%
1973	Rollason and Hall[18]	18%
1974	Plowman, Thomas and Thurlow[22]	14%
1979	Alexander and Murtagh[1]	12%
1980	Wright[17]	33%
	Whitehead, Whitmarsh and Horton[18]	60%
1981	Barker and Briscoe[12]	22%
1983	Hanna, Heap and Kimberley[20]	43%

This study was undertaken as a result of the clinical impression that dental patients anaesthetised with halothane developed fewer dysrhythmias after premedication which included droperidol than those given premedication containing hyoscine. The aim of this investigation was to assess the feasibility of modifying our standard anaesthetic technique for inpatient dental surgery, in order to reduce the incidence of dysrhythmias without the need for supplementary cardioactive drugs.

Methods

One hundred and twenty-three patients admitted to St Pancras Hospital for dental extractions, mainly of impacted third molars, were studied. Patients who were

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not ASA category 1 were excluded. Local ethical committee approval was not sought, as the drugs and techniques to be used were already well established in current anaesthetic practice.

Premedication of papaveretum 10–20 mg, combined with a randomly allocated dose of either 0.2–0.4 mg of hyoscine or 2.5–7.5 mg of droperidol, according to body weight, was administered by intramuscular injection 60–90 minutes prior to the induction of anaesthesia. The anaesthetic technique was standardised; all anaesthetics were administered by the author, with the help of the same Operating Department Assistant. Anaesthesia was induced via an indwelling needle on the dorsum of one hand with 4 mg/kg of thiopentone, followed, at the disappearance of the eyelash reflex, by 1 mg/kg of suxamethonium. The trachea was intubated under direct vision with a non-cuffed red rubber nasal tube, and a vaseline gauze throat pack was inserted. Anaesthesia was maintained with 33% oxygen in nitrous oxide, supplemented with halothane 2% inspired concentration for 5 minutes, reduced to 1% thereafter. Spontaneous ventilation was allowed to resume using a Mapleson A system delivering a fresh gas flow of 100 ml/kg/minute in order to eliminate rebreathing of carbon dioxide.

An Oxford Miniature Tracker Box[12] was then attached to the patient using sternal and cardiac apical electrodes. This machine records the electrocardiogram onto cassette tape, after the method described by Holter.[13] During surgery, the electrocardiogram was monitored using an oscilloscope and simultaneously recorded onto cassette tape. The coded tapes were subsequently analysed blind in the Cardiac Department using a Reynolds Medical Pathfinder. This device is capable of 'learning' the patient's normal cardiogram and then detecting and printing any variation from the stored trace. Ventricular, or QRS-related events are detected with 97–99% accuracy;[14,15] the correlation coefficient between manually counted paper traces and tapes of the same ECG is between 0.89 for isolated ventricular extrasystoles and 0.98 for bigemini or ventricular tachycardia. Poor recordings produce around 0.1% artifact detection (mainly electromyogram noise from pectoral or intercostal muscles). Atrial events are detected less well by the machine, and depend upon a change of rate rather than detection of the P wave itself—this requires that the associated QRS complex is displaced by 25% from its expected position. Therefore, detection of P wave abnormalities relies upon observer vigilance to a large extent, and no figures are available for the accuracy of the machine itself in this respect.

In a group of 50 patients, end tidal carbon dioxide $P_{E'}CO_2$ tensions were measured using a Hewlett-Packard mainstream capnometer placed in the catheter mount and calibrated to zero with 33% oxygen in nitrous oxide and to 100% with carbon dioxide, both from the Boyle's machine outlet swivel. This was done in order to determine, first, whether there is any difference in steady state $P_{E'}CO_2$ between those patients receiving hyoscine and those receiving droperidol, and second, whether there is any correlation between $P_{E'}CO_2$ and the occurrence of dysrhythmias. In common with previous studies, we did not classify sinus tachycardia as a dysrhythmia.[15,16] Ventricular dysrhythmias, with the exception of isolated ventricular extrasystoles, were treated by discontinuing the halothane and changing the fresh gas mixture to 50:50 oxygen in nitrous oxide. Atrial dysrhythmias were only treated if they affected blood pressure.

Results were analysed for statistical significance using the Chi squared test, applying Yates' correction for continuity, and Student's *t*-test.

Results

The study groups were comparable in terms of age, sex and weight distribution (Fig. 1), although the incidence of dysrhythmias was not related to any of these variables.

End tidal carbon dioxide tensions. There was no statistically significant difference in steady-state $P_{E'}CO_2$ between the group receiving papaveretum with hyoscine ($P_{E'}CO_2$ 6.36, SD 0.48 kPa) and those receiving papaveretum with droperidol ($P_{E'}CO_2$ 6.36, SD 0.59 kPa) ($p > 0.5$). Similarly, there was no significant difference in steady-state $P_{E'}CO_2$ between those patients in whom a dysrhythmia did not occur ($P_{E'}CO_2$ 6.44, SD 0.76 kPa) and those who exhibited a dysrhythmia ($P_{E'}CO_2$ 6.24, SD 0.65 kPa) ($p > 0.05$).

Patients who exhibited purely atrial dysrhythmias did not have a statistically different $P_{E'}CO_2$ at the point at which their dysrhythmia occurred ($P_{E'}CO_2$ 6.15, SD 0.68 kPa) to those who exhibited ventricular dysrhythmias ($P_{E'}CO_2$ 6.74, SD 0.78 kPa) ($0.1 > p > 0.05$).

Premedication. The types of dysrhythmia exhibited during this study are shown in Table 2. Some patients exhibited more than one type of dysrhythmia. The use of droperidol instead of hyoscine was associated with a reduction in the incidence of all types of dysrhythmia from 43% to 23%. This is statistically significant at the 5% level ($p = 0.03$). However, although the group receiving hyoscine exhibited a larger number of combined atrial and ventricular dysrhythmias than those receiving droperidol, this is not statistically significant ($p = 0.38$).

Discussion

Many different techniques have been advocated to reduce the incidence of cardiac dysrhythmias during dental anaesthesia; for example prophylactic beta blockade,[18–20] pretreatment with intravenous lignocaine,[21] local blockade of branches of the trigeminal nerve[22] and the use of positive pressure

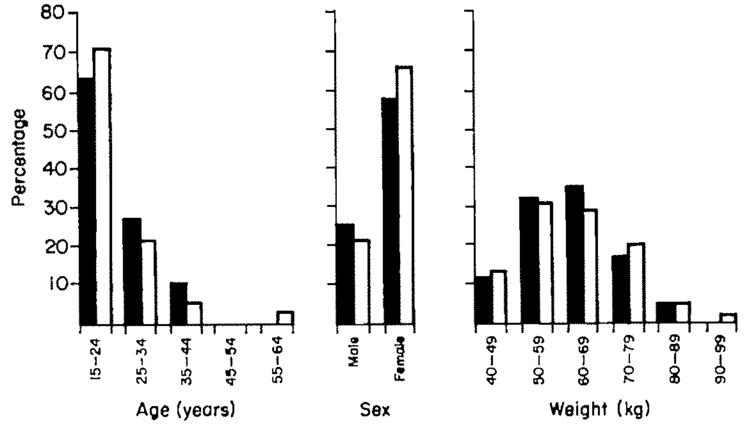

Figure 1. The percentage distribution of age, sex and body weight between the two study groups. ■, Hyoscine; □, droperidol.

Table 2. Distribution of the different dysrhythmias between the two study groups

	Papaveretum with droperidol	Papaveretum with hyoscine
Nodal rhythm	8	16
Atrial premature beat	1	1
Unifocal ventricular ectopic	2	4
Multifocal ventricular ectopic	2	2
Unifocal bigeminy	2	7
Multifocal bigeminy	0	1
Total	15	32

ventilation instead of spontaneous respiration during anaesthesia.[23] However, no method has gained widespread popularity, probably as a result of the questionable significance of the dysrhythmias. Bourne[24] considers that they are so common as to be a normal accompaniment of dental surgery, and that their significance is dubious in relation to a reported mortality of 1:15000. However, Kaufman[25] thought that they may precede sudden death. Tomlin[26] argued that the main cause of death is hypoxia rather than dysrhythmia, but it is to be hoped that significant hypoxia is not a common occurrence in current hospital inpatient practice. Plowman, Thomas and Thurlow[22] concluded that the dysrhythmias probably present few problems in fit patients, although they considered the theoretical possibility of an 'R on T' phenomenon triggering fatal ventricular fibrillation. Nevertheless, many of the techniques proposed for reducing dysrhythmias involve the additional administration of drugs which may themselves have untoward cardiovascular effects.

Mild hypercarbia probably plays no role in the genesis of cardiac dysrhythmias during oral surgery. Our figures for $P\text{E}'\text{CO}_2$ are similar to those of others who have demonstrated normal nor mildly elevated carbon dioxide levels in similar patients.[1,9,11]

This study indicates that the incidence of cardiac dysrhythmias during halothane anaesthesia may be dependent upon premedication. This lends support to the premise that anticholinergic agents facilitate the emergence of irregularities of cardiac conduction due to halothane. Droperidol is effective at preventing adrenaline-induced dysrhythmias,[27] and can be used to abort established dysrhythmias.[28]

A control group who received opiates were not included in this study because additional sedation was thought desirable for this group of young, fit but anxious patients. However, our results agree with those of Thurlow,[16] who demonstrated a significant fall in the incidence of dysrhythmias under halothane anaesthesia when a vagolytic was not used. In this respect, the combination of an anticholinergic premedication and halothane anaesthesia does not seem appropriate for patients undergoing dental procedures they are breathing spontaneously.

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Cardiac surgery in Jehovah's witnesses. A review of 36 cases

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Summary

Between January 1971 and January 1985, 31 Jehovah's witnesses underwent 24 bypass and 12 non-bypass cardiothoracic operations at the National Heart Hospital. Fifty-eight% of the group were under 16 years of age. There was one death in the non-bypass group unrelated to blood loss. Six deaths occurred in the bypass group. In one of these, blood loss contributed to the cause of death and in two patients, blood loss was directly related to the cause of death. The anaesthetic management of Jehovah's witnesses undergoing cardiac surgery is discussed.

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Key words

Complications; haemorrhage.
Organizations; Jehovah's witnesses.

The Jehovah's witnesses beliefs are based on the written word of the Bible, which they believe to be historically accurate; they reject all other philosophies and beliefs. As a direct result of their literal interpretation of the Bible, they will not accept transfusions of blood or blood products under any circumstances.[1-3] For this reason alone, they pose particularly difficult moral and ethical problems to surgeons and anaesthetists who may be required to look after them.[4,5] The management of their children is even more difficult and emotive.[6,7] Many are refused surgery because of their demands. Relatively few centres in the United Kingdom regularly undertake cardiothoracic surgery on Jehovah's witnesses, in view of the potential risk of major haemorrhage.

The authors are unaware of any study in the United Kingdom describing the management of these patients undergoing cardiac surgery. This paper reviews the experience at the National Heart Hospital of all cardiac operations undertaken on Jehovah's witnesses in the last 15 years.

Patients and methods

31 Jehovah's witnesses have undergone surgery at the National Heart Hospital since 1971. The majority of cases (70%) were seen after 1980, and the number referred annually is increasing. Of the 31 patients, there were 17 males and 14 females. Their ages ranged from 4 days to 67 years. Fifty-eight% of the group were under 16 years and 33% were under 5 years of age (Table 1).

Thirty-six operative procedures were performed on these patients; 24 of these were bypass and 12 non-bypass. Three patients had more than one operation. One child with a coarctation of the aorta repaired at age 3 months had a repeat repair at age one year. One patient had a catheter removed from his right atrium 3 weeks after an open mitral valvotomy. Another patient had three further operations: after a closure of single atrium and mitral valve repair, he underwent excision of a painful sternotomy scar, exploration of a wound sinus and, finally, removal of infected Teflon from his right atrium.

The procedures are listed in Table 2. All the data were obtained retrospectively by inspection of the patients' case notes. The anaesthetic technique was the same as that used in non Jehovah's witness patients undergoing similar procedures. Premedication comprised atropine alone in small infants. Older children received trimeprazine tartrate followed by papaveretum and hyoscine. Adults were given lorazepam followed by papaveretum and hyoscine, depending on the patient's age, weight and physical condition.

Table 1. Age distribution of patients in the study

Age	Number of patients
Under 1 month	1
1 month–1 year	5
1 year–5 years	6
5 years–16 years	9
Over 16 years	15

Table 2. Details of operations

Non-bypass procedures (12)		Deaths
Pulmonary valvotomy	3	
Coarctation of the aorta	2	
Coarctation of the aorta, patent ductus arteriosus, pulmonary artery banding	2	
Modified Blalock shunt	1	1
Removal catheter right atrium	1	
Excision sternotomy scar	1	
Exploration wound sinus	2	
Bypass procedures (24)		
Coronary artery vein graft (CAVG)	8	2
Mitral valve replacement	2	1
Mitral valvotomy	2	1
Aortic valve replacement	1	
Pulmonary valve homograft and repair ventricular septal defect	1	
Aortic valve homograft	1	
Atrio-ventricular canal repair	1	
Repair Fallot's tetralogy	1	
Switch repair for transposition of the great arteries	1	1
Ebsteins anomaly	1	
Mustard procedure	2	
Repair aortopulmonary window	1	1
Right ventricular reconstruction	1	
Repair single atrium	1	

Anaesthesia was induced with cyclopropane and oxygen for small children; adults received either thiopentone or methohexitone. Muscle relaxation was provided by pancuronium, and maintenance of anaesthesia was with nitrous oxide, oxygen and analgesic supplements of either fentanyl or papaveretum. In the bypass group, and where appropriate in the non-bypass group, invasive monitoring was employed. This consisted of a percutaneous arterial line and two or three internal jugular lines. Additional monitoring was provided by an ECG, a nasopharyngeal temperature probe and a urinary catheter. A nasogastric tube and a peripheral intravenous infusion were routine.

In all patients with an adequate pre-operative haemoglobin, a unit of blood was taken into a CPD-adenine transfer pack before bypass. Two units were taken if the pre-operative haemoglobin was normal or raised; less was taken in children. The fluid taken was replaced with Ringer lactate BP or polygeline. This blood was always connected to the patient although the line was clamped during cardiopulmonary bypass.

Bubble oxygenators were used in the majority of cases (BOS-10, BOS-5, Shiley 070). The prime was Ringer lactate BP solution in all cases. A reduced prime would be used if the patient's pre-operative haematocrit was low. A prime of 1.5 litres (500 ml reduction) was frequently employed during adult bypass. In all cases, the prime was sufficient to maintain safe and adequate equilibrium levels during bypass. Heparin 3000 IU/litre was added to the prime. In children, the dilution during bypass was calculated and the haematocrit predicted. If this was low, then reduced prime and minimal volume tubing was used. It may also be possible to use narrower bore tubing if the increased resistance to flow is within acceptable limits. Moderate hypothermia (25°C) was used in all but the shortest cases. Ice cold cardioplegia or coronary artery perfusion was used where appropriate for myocardial protection. After bypass the heparin was reversed with protamine.

The pre-operative haemoglobin and haematocrit were estimated on the day before surgery in all cases. The lowest haemoglobin and haematocrit values were recorded between the first and sixth postoperative day and were used to calculate the maximum percentage fall in haemoglobin. The postoperative losses were measured up until the time the drains were removed. This was usually within 24 hours of the end of surgery.

All patients signed consent forms which specified their wishes regarding the use of blood or blood products. The majority demanded that no blood be used under any circumstances. In the bypass group, two patients agreed to the use of plasma but not blood and three patients agreed that blood could be used under life threatening circumstances.

Results

Non-bypass group. The blood losses in the noncardiac cases were recorded as being minimal and have not been included in the results. The changes in haemoglobin and haematocrit values that occurred are summarised in Table 3. The mean volume of fluid infused peroperatively was 2 ml/kg per hour. The mean peroperative urine output, when measured, ranged from 15–540 ml. The mean operative time was 135 minutes. The mean postoperative blood loss was 11.2 ml/kg (SD 10.45). Four patients had losses that exceeded 10% of estimated blood volume (70 ml/kg).

There was one death in this group which was unrelated to blood loss. A three and a half-year-old boy with pulmonary atresia (haemoglobin 14.1 g/dlitre) had a modified Blalock shunt. On day 5 postoperatively, he developed severe pulmonary oedema and cardiac arrest. His haemoglobin was 11.1 g/dlitre at this time. He made a poor recovery and died on day 9.

Bypass group. In two patients, a cell saver was used and these results have been analysed separately. The changes in haemoglobin and haematocrit that occurred are presented in Table 4. The mean volume of fluid infused peroperatively was 1400 ml (SD 800). The mean peroperative urine output was 4.75 ml/kg per hour (SD 2.03). The mean operative time was 313 minutes (range 180–480 minutes). Mean bypass time was 100 minutes (range 35–280 minutes). The postoperative blood losses were greater than the non-bypass group, with a mean value of 13.2 ml/kg (SD 9.3). Six patients had postoperative losses of greater than 20% of estimated blood volume. Four patients had haematocrits below 20% in the early postoperative period. One of these was transfused with blood (consent obtained pre-operatively), two patients died and the fourth recovered uneventfully.

Table 3. Changes in haemoglobin and haematocrit in the non-bypass group ($n = 12$)

	Haemoglobin (g/dlitre)		Haematocrit (%)	
	Mean (SD)	Range	Mean (SD)	Range
Preoperative	13.14 (3.26)	8.2–19.3	39.5 (10.0)	25–60
Lowest postoperative reading	10.1 (1.16)	7.6–12.2	30.0 (3.5)	22–34
Result day one postop	11.7 (1.9)	8.9–15.6	34.8 (5.6)	27–47
Result day two postop	10.3 (2.0)	7.7–13.1	30.8 (7.08)	22–41
Maximum percentage fall	23.7 (13.8)	7.0–47	24.6 (14.0)	7–49

Table 4. Changes in haemoglobin and haematocrit in the bypass group ($n = 24$)

	Haemoglobin (g/dlitre)		Haematocrit (%)	
	Mean (SD)	Range	Mean (SD)	Range
Pre-operative	14.1 (2.61)	10.9–19.8	40.2 (14.29)	29–56
Lowest postoperative	7.66 (3.7)	2.4–12.1	24.8 (7.25)	8–35
Result day one postop	9.9 (1.98)	7.4–14.1	29.9 (7.1)	22–43
Result day two postop	9.0 (1.8)	6.9–11.2	27.2 (4.64)	20–36
Maximum percentage fall	42.0 (16.1)	26–83	39.2 (18.3)	7–81

The two patients who had agreed to the use of plasma were give plasma both during and after surgery. Two of the three patients who agreed to blood if necessary, were given blood. The first was a 19-year-old male for aortic homograft surgery whose peroperative losses were large; he received four units of blood. The second patient was a 5-year-old having an atrioventricular canal repair. Her mother was a Jehovah's witness, but her father was not. In the recovery ward, her haemoglobin was 5.0 g/dlitre and she was given blood.

There were six deaths. In three patients the cause of death was unrelated to blood loss. Two failed to come off bypass and the third died of cardiogenic shock in the early postoperative period, with a haemoglobin of 11.4 g/dlitre. In one case, anaemia secondary to blood loss contributed to the cause of death. This case was a 60-year-old female who required a repeat mitral valve replacement. Pre-operatively she had poor left ventricular function, with a haemoglobin of 11.3 g/dlitre and haematocrit 34%. Postoperatively she required large doses of inotropes. She had episodes of ventricular tachycardia and ventricular fibrillation, low blood pressure (70–90 mmHg) and required intermittent positive pressure ventilation throughout her stay in the intensive care unit. Postoperative blood loss during the first 48 hours was 1600 ml, which was replaced with polygeline. Her haemoglobin remained between 7.5 and 8.5 g/dlitre (haematocrit 23–26%) throughout. She died on day 12.

In two patients, acute blood loss was directly related to the cause of death. The first was a 10-month old female weighing 5.5 kg for closure of an aortopulmonary window. Pre-operative haemoglobin was 11.6 g/dlitre (haematocrit 35%). Surgery was uneventful. Postoperative blood loss during the first 24 hours was 160 ml. On day one her haemoglobin was 3.7 g/dlitre. Cardiac arrest occurred despite tracheal intubation and continuous positive airway pressure and she could not be resuscitated.

The second was a 56-year-old female for open mitral valvotomy. Pre-operative haemoglobin was 14.0 g/dlitre (haematocrit 42%). Three hours postoperatively she began to bleed from her chest drains and rapidly lost 800 ml. Her chest was opened on the intensive care unit and she was found to have tamponade from a tear in the left atrial appendage. At this stage the haemoglobin was 2.4 g/dlitre (haematocrit 8%). Drainage blood was filtered and re-infused. Her pupils became fixed and dilated. Her husband reluctantly agreed that donor blood could be given. In spite of inotropes, artificial ventilation and blood, her general condition did not improve. She developed renal failure and died on day 5.

Use of cell saver. Two children with transposition of the great arteries underwent a Mustard operation. A cell saver (Haematinecs) was used to collect blood lost peroperatively. The blood is filtered and the red blood cells separated. The cells are then washed, suspended in saline and re-infused after bypass. The system is so arranged as to form a continuous circuit and this is acceptable to Jehovah's witnesses in the same way as the bypass circuit.

The first child weighed 5.8 kg and had a pre-operative haemoglobin of 16.1 g/dlitre. This was 12.5 g/dlitre on day one and 11.7 on day two. The maximum decrease in haematocrit was to 32%. The second patient weighed 15 kg and had a pre-operative haemoglobin of 16.8 g/dlitre, which fell to 14.3 on day one and 12.8 on day two. The maximum decrease in haematocrit was to 30%.

Discussion

In the early days of open heart surgery, fresh donor blood was used to prime the pumps and oxygenators for bypass. The difficulties of providing large quantities of fresh blood together with the problems secondary to bypass with blood as a prime prompted workers to use a non blood prime.[8-12] It was found that the blood losses during open heart surgery were frequently quite small. There followed numerous reports to confirm that many patients undergoing open heart surgery do not require blood during or after bypass.[13-19] As a result of this evidence, reports appeared of open heart surgery in Jehovah's witnesses, where a pre-operative decision not to use blood was made.[20-24] The feasibility of such procedures was thus established. The majority of these studies have been in the American surgical literature, which reflects the greater number of Jehovah's witnesses in North America. There have been several reports highlighting the difficulties encountered either during major surgery or after acute severe haemorrhage in these patients without the provision of blood transfusion.[25-31]

The haemodilution secondary to the use of a crystalloid prime has several advantages. There is a reduced need for fresh donor blood and a reduction in the risks secondary to blood transfusion. Provided that normovolaemia is maintained, oxygen delivery to the tissues is not impaired by a reduction in the haematocrit to between 25 and 30%.[32-35] During bypass, provided a high flow is maintained, a haematocrit of 20% is acceptable.[36] After open heart surgery, the advantages of a reduced blood viscosity and improved tissue oxygenation still apply, provided that the cardiac output and blood oxygen saturation are maintained. If the cardiac output is impaired, the situation is less satisfactory. In patients with anaemia and poor myocardial function, it is essential to maintain optimal gas exchange and mimimise oxygen consumption. To this end it is advisable to maintain paralysis and positive pressure ventilation until myocardial function is optimal and inotropes are no longer required.

Future management may be improved by the use of oxygen carrying fluorocarbons which will facilitate more profound haemodilution. However, the treatment of severe haemorrhage is not only concerned with oxygen transport, but frequently requires the administration of platelets and clotting factors which are unacceptable to Jehovah's witnesses.

The mortality in our series is high. Other published work[20–24] has shown that cardiac surgery in adult Jehovah witnesses may be carried out with acceptably low risk. The largest series describes 362 cases with an early mortality of 10.7%.[21] This study had less paediatric work than ours and the authors stressed that surgery is not recommended in children if large losses are expected. It is significant that the National Heart Hospital has a large number of patients referred from other cardiac units. The number of high-risk patients is therefore larger than would be expected in such a small study. The overall mortality is also affected by those patients in whom blood loss without transfusion contributed to the cause of death. Three patients came into this category.

The management of Jehovah's witnesses can be made optimal by a clear plan of action (see appendix). It is particularly important that the patient or legal guardian signs a specific consent form which details their demands concerning blood transfusion. In this way it is possible to find out if the patient will accept any of the alternatives to donor blood such as the predeposition of their own blood or the use of blood products. Most will not accept blood, but there appear to be varying degrees of commitment and some will accept blood products. It is also possible that they may change their mind following severe haemorrhage.[37] In the case of children, the doctor must choose how he can protect both the interests of the patient and his own conscience. It is the policy of the Board of Governors of the National Heart Hospital not to make these children wards of court. The Medical Defence Union and the Medical Protection Society are also not in favour of making these children wards of court. They recommend that the doctor does what he thinks is right at the time. The defence organisations will support the doctor, whatever his course of action.[6] Possibly the statistics and controls that lead us to choose the surgical option in treatment are not valid in such people. Our study suggests that when the important option to use blood is removed; the occasional risk of death from severe haemorrhage is ever present. Any doctor who undertakes by-pass surgery in Jehovah's witnesses is taking a calculated risk that blood will not be required.

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Appendix 1

Current policy for the anaesthetic management of Jehovah's witnesses at the National Heart Hospital.

1. Ensure adequate pre-operative haemoglobin. Treat pre-operative anaemia with appropriate supplements and delay operation.
2. Discuss the patient's specific demands regarding infusions. These may vary from patient to patient. In particular ask

   a) Will you accept blood under any circumstances?
   b) Will you accept plasma/plasma protein fraction?
   c) Will you allow predeposition of blood in storage?

3. Sign specific consent which states wishes.
4. Use standard anaesthetic technique.
5. Use haemodilution.
6. Reduced prime if predicted bypass haematocrit will be low.
7. Minimum tubing and consider small bore in children.
8. Meticulous surgical technique—careful haemostasis.
9. Autotransfusor or cell saver where appropriate.
10. Fully reverse heparinisation with protamine.
11. Oxygen and IPPV postoperatively until myocardial function optimal.
12. Re-explore early in the event of continued losses from wound drains.
13. Iron, B_{12} and folate supplements postoperatively.

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Plasma morphine levels produced by continuous infusion in children

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Summary

Blood samples were taken from six children aged between 10 months and 15 years, at intervals over a period of 40 hours while they were receiving continuous morphine infusions. The plasma morphine values obtained showed similar and consistent levels 15–30 minutes after starting the infusions.

Key words

Analgesics, narcotic; morphine.
Pain; postoperative.

Continuous morphine infusions have been used for a number of years in the Fleming Hospital for Sick Children, to provide postoperative pain relief in children.[1] This study was undertaken to determine the plasma morphine levels reached over a period of 40 hours from the start of the infusions. Informed consent to the investigation was received from the parents, and from the children old enough to understand the implications.

Method

Six children between the ages of 10 months and 15 years received continuous infusions of morphine following major surgery. All of the children had received premedication of morphine 200 μg/kg and atropine 15 μg/kg intramuscularly about an hour before operation. All the children received a general anaesthetic during which no further narcotics were given. During the anaesthetic, a cannula for the morphine infusion was inserted into a peripheral vein and a sampling cannula was inserted into a limb vein free from any infusions.

Following the operation, the children were returned to the ward and a control sample of 2 ml of blood was taken from the sampling cannula. A loading dose of 200 μg/kg body weight of morphine was then given through the morphine infusion cannula and the infusion started immediately. This consisted of 50 ml of normal saline containing 1 mg/kg body weight of preservative-free morphine delivered at a rate of 1 ml/hour with a Vickers Treonic syringe pump, thus delivering 20 μg/kg/hour of morphine. Blood samples were taken at 2, 4, 8, 15 and 30 minutes and 1, 2, 4, 8, 16, 24, 32 and 40 hours after the start of the infusion. Each blood sample was centrifuged as soon as possible and stored at −18°C until assayed.

Plasma morphine levels were assayed using a commercially available solid phase radio-immunoassay (Coat-A-Count, Diagnostic Products Corporation, Wallingford, UK) with a low cross-reactivity (0.22%) to morphine 3 glucoronide. The assays were performed in accordance with the manufacturer's protocol with the following alterations. In place of the manufacturer's standards, human plasma based standards were used with morphine concentrations of 0, 1, 5, 10, 25 and 100 μg/litre. The assays were performed on the original plasma samples and also on a ten-fold dilution in drug-free human plasma. In all cases, a 25 μg/litre aliquot was used and the assays were performed in duplicate. The coefficient of variance was 7% for 'run to run' assays and for 'within run' assays this was 7.7%, 6.0% and 6.1% for laboratory standards of 20, 50 and 100 μg/litre respectively.

Results

The results from the six patients, together with the mean plasma level for each sampling time and their standard deviations, are shown in Table 1. The mean plasma levels of the control and the samples taken after 15 minutes are shown in Fig. 1.

It was decided that the results of the 2-minute sample showed that incomplete mixing had occurred. Difficulties were encountered taking samples from patient 2 at 16 and 24 hours and these results were discarded. Patient 3 required a top-up bolus dose of 100 μg/kg immediately after the 24-hour sample. With this

Table 1. Plasma morphine levels (ng/ml) produced by continuous infusion in children

	Time of sample													
	Minutes						Hours							
	C	2	4	8	15	30	1	2	4	8	16	24	32	40
Patient 1	<5	336	465	133	68	49	34	26	18	15	15	14	14	15
2	12	142	83	65	51	45	32	27	19	18	—	—	14	14
3	11	650	295	130	76	56	35	22	19	14	14	12	—	—
4	12	134	750	139	83	57	33	27	17	12	13	13	19	10
5	10	121	486	160	69	49	38	26	19	17	16	20	19	21
6	16	130	600	136	90	54	47	34	27	22	23	22	24	23
Mean	11	—	446	127	73	52	37	27	20	16	16	16	18	17
SD	4	—	233	32	14	5	6	4	4	4	4	4	4	5

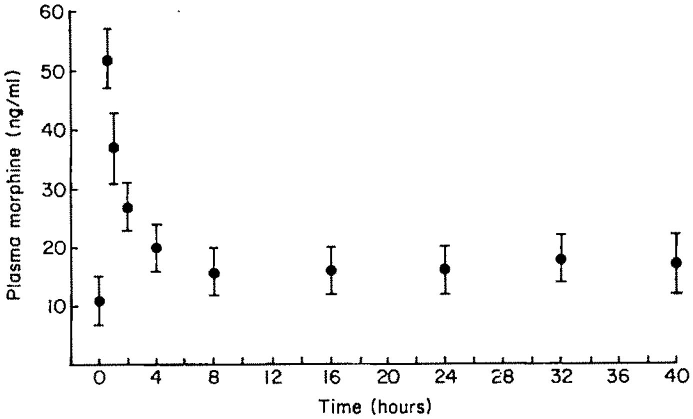

Fig. 1. Mean (SD) plasma morphine levels of the control sample and of samples taken from 30 minutes to 40 hours after the start of the morphine infusions.

exception, all the children achieved satisfactory pain relief from their morphine infusion, as indeed did patient 3 after receiving the top-up.

Discussion

Continuous morphine infusions were started in our hospital because of dissatisfaction with intermittent, as required, morphine and the obvious difficulties in using patient controlled analgesia in small children. The infusions have been shown to produce better and more consistent pain relief in children than as required morphine.[1] This present study shows that from 30 minutes, the plasma morphine levels are similar in different patients and from 8 hours become reasonably constant, with a mean level of 16–18 ng/ml.

These results suggest that continuous infusions of morphine, calculated only on a body weight basis, produce fairly consistent plasma morphine levels. It takes no account of any differences in plasma levels that might be needed to produce adequate pain relief in different patients, which patient controlled analgesia appears better able to produce. It is, however, a simple and cheap system which can be used in small children unable to operate a patient controlled system.

Acknowledgments

The authors would like to thank Dr G. Dale for his advice during the course of this study. Figure 1 was produced by the Audiovisual Department, University of Newcastle upon Tyne.

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Short by default

We, as consultants in a District General Hospital, are becoming increasingly concerned at the difficulty we experience in recruitment at the registrar grade. Basingstoke has a busy District General Hospital with eight juniors and eight consultants. There are four consultant sessions in obstetric anaesthesia, a consultant is in charge of the intensive care unit, with two sessions devoted to this, and two anaesthetists are in charge of a comprehensive pain relief service. We have a senior registrar rotation to the teaching hospital in Southampton and have the added bonus of two thoracic surgical lists per week.

Our own trainees are extremely happy, as have been their predecessors. Study leave is hardly ever refused and we are fortunate to employ locum Consultants during Consultant annual leave. Faculty recommendations made in the past have been fully carried out, to the letter. So why are we experiencing this difficulty in recruitment? It would appear, that trainee anaesthetists are reluctant to accept a Registrar post in the periphery in case they have difficulty in returning to a teaching hospital. Do the teaching hospitals wish to have sole control of the training of all anaesthetists above senior house officer grade? Surely, there is valuable experience to be gained in working in a District General Hospital. Most of these trainees will themselves be Consultants in a District General Hospital when their training is complete.

If registrar training is restricted to the teaching hospitals, registrar posts in District General Hospitals will remain vacant and will be replaced by consultant posts. The Short Report[1] will be implemented by default and consultants will have to be resident on duty to cover obstetric departments and intensive care units. Our teaching hospital colleagues will, of course, be immune from this, since they will have the sole responsibility for training and will have ample trainees to cover the on-call commitments. If this is the face of anaesthesia in the future, it is totally unacceptable. A reduction in the junior grades and an increase in the number of consultants is necessary if career prospects are to be improved, but this must be done in a way that is acceptable to all anaesthetists.

We would offer two suggestions for consideration by the Faculty which might help to solve this problem. Firstly, all teaching hospital registrar posts should rotate with a District General Hospital. Secondly, it should be a requirement for accreditation that a period of 1–2 years be spent at both registrar and senior registrar grade in an approved District General Hospital. This would not only improve staffing in the District General Hospitals, but would provide a more balanced career structure for those who will ultimately be consultants therein.

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A comment from the Dean of the Faculty

Thank you for allowing me to see this letter and I thank the authors for their comments.

Many factors are operating to affect recruitment, career prospects and manpower at the present time. In response to these, the Faculty recently set up working groups, in conjunction with the Association of Anaesthetists, in an attempt to solve these and similar problems. Additionally, both the Faculty's Hospital Recognition Committee and also the Joint Committee for the Higher Training of Anaesthetists keep their procedures under continuous review. The suggestions in this letter are eminently sensible and are amongst those under discussion.

The Hospital Recognition Committee encourages rotations between teaching and district hospitals, and in some cases recognition is dependent on them. An integrated regional pre-fellowship training scheme is attractive, although the practical difficulties should not be underestimated. Where it has been implemented, it seems to work well, but at the cost of restricting the trainees' choice of where they work and the consultants' choice of their own junior staff. For Higher Training leading to Accreditation, almost all the approved programmes do already include such rotations.

Manpower is at present under close scrutiny and I should like to take this opportunity of encouraging Fellows to write directly to me about recruitment and staffing problems, but only where such information can be backed up by adequate data which helps the Faculty to conduct its negotiations with the Government and DHSS.

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Aseptic versus no-touch cannulation

A recent report from this Department[1] showed that there was no difference in the rate of bacterial contamination and infection between a central venous (internal jugular) cannula protected by full asepsis during insertion and one protected by a plastic sleeve.[2] Unfortunately, I did not have the opportunity of seeing the manuscript before publication and a critical Editorial in the same issue[3] also failed to emphasise that both techniques can safeguard the cannula from bacterial contamination in this series, apparently with equal efficacy. Other workers have also overlooked this important point[4] and there has been some adverse criticism of our methods. *Unprotected* cannulae are still widely used for jugular cannulation and inserted virtually without asepsis but, in my view, this is quite unacceptable today. Another study in this context might well show a great difference between a clean and a dirty method. All we can say at the moment is that a plastic sleeve can provide the same protection as an aseptic approach and is swifter and less laborious, important advantages in critical situations.

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A reply

Dr Gilston's defence of the paper by Clayton and his colleagues and in favour of his cannula is misleading. The study by Clayton proves nothing at all. The number of patients was far too small and the observations did not cover, in sufficient number, the period after 48 hours, when the infective complications of intravenous cannulation begin to become serious.

What is, in my view, much more serious is the way in which the conclusions of this inadequate study tend to undermine the foundations of long established practice. There can be little argument about the expedient techniques that may be appropriate in critical situations, but Clayton's patients were being subjected to elective (premeditated!) procedures. The casual reader may, therefore, conclude that provided no-touch techniques are used, aseptic technique, in particular the washing of hands, can be neglected. In fact no-touch is an inherent part of aseptic technique. Aseptic routines cannot be observed only in part without risk. Variations in routine lead to error in the routine. There are as many examples of the truth of this general proposition in the practice of anaesthesia as there are in the practice of preventive microbiology.

I am horrified by Dr Gilston's claim that 'unprotected cannulae are still . . . inserted without asepsis'. He regards this as unacceptable; I stand by my editorial.

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Continuous infusion epidural analgesia in obstetrics

Ewen *et al.* (*Anaesthesia* 1986; **41:** 143–7) regard an epidural infusion of 25 ml/hour of 0.08% bupivacaine (20 mg/hour) for labour as satisfactory. We are concerned about the implications of their regimen for patient safety, in particular in the event of accidental intrathecal infusion.

An acceptable system using epidural infusion must be a compromise between efficacy and safety. In an effort to obtain the best balance, our study[1] proposed a regimen of 10 ml/hour of 0.125% bupivacaine (12.5 mg/hour). We have recently completed studies in a further 50 patients who required an epidural block for an average duration of 420 minutes; a total of 70 primigravid mothers have now been studied.

A striking feature is the difference in the incidence of high blockade. Our lower dose regimen resulted in only one patient having sensory loss *up to* T_4 with the remainder below T_6, while one third of Ewen's mothers had a block extending bilaterally *above* T_4. This is a disadvantage. Moreover, with the larger dose, should the epidural catheter pass intrathecally, the block would extend more rapidly. Indeed, we recommend that a test of sensory level at T_6 should be carried out every 2 hours. The technique of Ewen *et al.* would lead to many calls for the anaesthetist!

Our regimen resulted in 76% mothers who required no (32%) or only one (44%) top-up, compared to their 60% (15 mothers) who required no top-up. Is that advantage worth more risk?

Ewen and his colleagues also suggest that their regimen would reduce the incidence of hypotension by reducing the number of top-ups, but their results show the opposite. In the group with fewer top-ups (mean 0.6/patient) 12 hypotensive episodes were recorded. In the other group (mean top-ups 1.32/patient), there were five episodes of hypotension.

Analgesia in labour should be as free from hazard as possible, while still remaining reasonably effective. Epidural infusions of local anaesthetic agents are a promising development, but safety should not be compromised in too tight a trade-off with the number of top-ups.

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Reference

1. Li DF, Rees GAD, Rosen M. Continuous extradural infusion of 0.0625% or 0.125% bupivacaine for pain relief in primigravid labour. *British Journal of Anaesthesia* 1985; **57:** 264–70.

A reply

Thank you for the opportunity to comment on this letter. Continuous epidural infusion of 0.08% bupivacaine for labour has now been used in 1687 mothers in Aberdeen. With regard to accidental intrathecal administration we think it is unlikely that an infusion, which at the maximum rate takes 37 minutes to deliver 12.5 mg bupivacaine, can be less safe than an accidental delivery by top-up (bolus) injection of a much greater dose. We believe that patient safety is improved by our technique.

Except for the 53 cases in our published investigation, we do not make formal checks for height of block every 2 hours. This time interval is too infrequent to be useful in the detection of accidental intrathecal infusion. We ask the mothers to report the occurrence of numbness extending to the chest or the breasts. The midwife then switches off the infusion and calls the anaesthetist. The few patients who are unable to cooperate in this require special supervision. In fact, we have relatively few calls for the anaesthetist.

It should be noted that in their recommended procedure,[1] only 21% of mothers required no top-up, whereas in our series of longer duration, 60% of mothers required no top-up during the infusion. Any reduction in the number of top-ups will improve safety.

With regard to the incidence of hypotension in our series, it can be seen that all but one of the top-up related episodes followed the initial bolus injection. We have caused misunderstanding by using the term top-up to include the initial bolus injection as well as subsequent bolus injections. Hypotension, not related to top-ups, occurred in only two patients in either Group A or B; (A, 0.08%, B, 0.25% bupivacaine at 20 mg/hour). We do not routinely preload all our patients with an intravenous infusion of Hartmann's solution.

We believe that the safest way to administer epidural analgesia in labour is by continuous pump infusion. Bupivacaine 0.08% delivered up to a maximum rate of 25 ml/hour continues in our experience to be very satisfactory.

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Continuous pump infusion epidural analgesia offers the clear advantage of smooth analgesia over intermittent top-up procedures. However, in the greater interest of patient safety, the choice of dose rate requires careful consideration. At 20 mg bupivacaine/hour, as described by Ewen *et al.* (*Anaesthesia* 1986; **41**: 143–7) the incidence of side effects is disturbingly high. At a lower dose rate, effective analgesia can be provided with minimal side effects.[1–4]

In Dr Ewen's series, the 25 patients in Group A received 0.08% bupivacaine at 20 mg/hour. There were 12 hypotensive episodes in this group. Eight of these 25 patients had bilateral segmental analgesia above T_4. Approximately 50% of Group A patients had severe motor weakness. Only five out of 25 deliveries were spontaneous (and seven out of the total 53 patients). Such intensity and extent of blockade is surely not necessary for analgesia of the labouring mother, and calls into question the safety of the dose regimen. It is worrying that one of the four mothers in Group A (and two out of 10 in Group B) who required Caesarean section had such profound blockade that surgery was performed without supplemental top-up. Ewen *et al.* have shown that increasing the volume infused extended the blockade, but at a dose rate of 20 mg/hour using 0.08% in a third of the patients the block was surely too extensive.

Like Li *et al.*,[2] we have found that an infusion of 0.125% bupivacaine at 10 ml/hour is optimal. We studied 45 patients receiving such an infusion during labour, after the establishment of an epidural using 3 ml (test dose) plus 12 ml 0.25% bupivacaine plain. Eighty percent of patients required none or only one top-up of infusion for a mean infusion time of 7 hours until delivery (range 3–13.5 hours); top-up = 10 ml bolus of infusate. Twenty-five patients had good pain relief with the infusion alone for a mean infusion time of 6.5 hours until delivery (range 3–12.5 hours). There were no hypotensive episodes (blood pressure was monitored and recorded using a Datascope Accutor initially at 5-minute and then 30-minute intervals.) No patient had motor blockade intense enough to prevent them turning themselves; this is an advantage which contributes to maternal well-being and is labour-saving. Sixteen of our 45 patients had spontaneous vaginal deliveries; no patient had blockade as high as T_4.

The safety of such a regimen has already been stressed by Li *et al.* and they have shown that increasing the dose rate above this confers no additional advantage.[2] In the interests of safety we feel that the infusion of bupivacaine should be set up at the lowest safe and effective dose rate. Our findings agree with those of Li *et al.* that 0.125% bupivacaine at 10 ml/hour is optimal, but further studies to evaluate 0.08% at a lower dose rate would be valuable.

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A reply

Thank you for the opportunity to respond to this letter. We agree that continuous pump infusion epidural analgesia offers the clear advantage of smooth analgesia over intermittent top-up procedures. It also has the advantage of greater safety. Bupivacaine at the initial dose of 20 mg/hour was the rate we studied in our paper. Our study was not designed to seek the optimal dose rate. We have not claimed that 20 mg/hour is the correct rate for every patient. The point of our paper was that the 0.08% solution was more effective than the 0.25% solution of bupivacaine. Presumably, a wider segmental spread is maintained. We have continued with the use of a 0.08% solution of bupivacaine in Aberdeen because we have found it very satisfactory (in over 1700 mothers now). This may indeed not be the optimum dilution. Provided the dose rate of bupivacaine is adequate, greater dilution may be even more satisfactory!

We agree with the suggestion that a further study of the 0.08% solution at a lower dose rate could be valuable. Bupivacaine 12.5 mg/hour is considered the optimal dose rate by the authors of the two letters written in response to our paper. Optimal dose rate is the balance between that which achieves adequate and uninterrupted pain relief and that which at the same time produces a minimum of unwanted side effects such as hypotension.

The balance point is influenced by patient demand. The great majority of our patients do not wish to feel any pain at all once the epidural is established. During the period April to December 1985, 426 mothers in the Aberdeen Maternity Hospital, who had singleton vertex vaginal deliveries and continuous infusion epidurals, were questioned during labour with regard to their views on spontaneous vaginal delivery. They were asked if they wanted the epidural infusion switched off when they were considered to be at full cervical dilatation so that they could push with the contractions. This would increase the chances of delivery without forceps. The answers were yes 18%, no 73%, and don't know (or didn't understand) 9%. The spontaneous delivery rate was 34%, 33% and 24% in each group respectively.

With regard to the incidence of hypotension, we have already commented that it was usually associated with the initial bolus dose.

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Cross-sensitivity between relaxants

We wish to comment on the letter from Dr Watkins and Professor Nimmo (*Anaesthesia* 1985; **40:** 813–25) which contains two statements which are not supported by the evidence available. It is true that many people have reservations about intradermal testing in the diagnosis of severe anaphylactoid reactions during anaesthesia, but the diagnostic value of such testing has been confirmed in at least eight series and numerous anecdotal cases. Its value as a predictive test in patients without history of a reaction is, as your correspondents suggest, of less value.

To state that cross-sensitivity between relaxants is not proven depends on what constitutes proof. Absolute proof would require the administration of different relaxants to a patient as sole agent at different times to produce severe reactions. This is obviously ethically untenable. However, there is overwhelming supportive evidence that such cross-sensitivity exists from at least eight clinical reports, intradermal studies,[1–4] leucocyte and basophil histamine release[1–5] and more recently radioimmunoassay.[6] Indeed, the demonstration that the quaternary and tertiary ammonium groups, common to muscle relaxants and necessary to provide neuromuscular blocking activity, are the antigenic groups on the muscle relaxant[7] would make it extremely surprising if such cross-reactivity did not occur. Failure to appreciate the possibility of cross-sensitivity between muscle relaxants has been identified as a cause of second reactions.

(At the request of the Editor an abbreviated bibliography has been provided, a full list of supporting references may be obtained from Dr M. Fisher).

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An unusual complication of thiopentone administration

This is a report of an unusual case of radial nerve palsy following intravenous thiopentone administration. A 17-year-old girl presented with acute appendicitis and an emergency appendicectomy was planned. She had no previous medical history of any note and had never undergone general anaesthesia. Ninety minutes after premedication with papaveretum 15 mg and hyoscine 0.3 mg she arrived in the anaesthetic room. A 23-gauge butterfly needle was inserted into a vein on the dorsum of her right hand. She was pre-oxygenated and 325 mg (13 ml) of 2.5% thiopentone was injected. To my surprise this had no effect; there was no extravasation of thiopentone around the venepuncture site and the patient did not complain of any discomfort. The syringe in use was substituted for another which had previously been drawn up and a further 125 mg (5 ml) of thiopentone was injected. This also had no effect. Another 23-gauge butterfly needle was inserted into a vein on the dorsum of her left hand and when 250 mg (10 ml) of thiopentone was injected via this route anaesthesia was rapidly induced. This was followed by suxamethonium 100 mg, with the application of cricoid pressure, and the patient was intubated. Anaesthesia was subsequently maintained with enflurane 0.8% in 66% nitrous oxide and 33% oxygen by intermittent positive pressure ventilation and relaxation with alcuronium 15 mg. It was possible during the operation to withdraw blood quite easily from the right hand butterfly which suggested that this needle was inside a vein.

The patient recovered satisfactorily from the operation. However, on the day following the operation she noticed a moderate swelling of her right forearm and hand. She was also aware of a weakness of right hand grip and, in particular, extension of her right thumb and index finger. There was no associated numbness. She was seen by a consultant neurologist who confirmed that she had weakness in extensor pollicis longus and extensor indicis. Fortunately, over the following 2 months, the swelling in her forearm and hand gradually subsided and the power to her extensor muscles returned.

Extensor pollicis longus and extensor indicis muscles form part of the deep group of muscles in the posterior fascial compartment of the forearm; they lie side by side and have origins on the posterior surface of the ulna and the interosseous membrane. Their nerve supply comes from the deep branch of the radial nerve, which supplies motor branches to the muscles in the compartment and articular branches to the carpus.[1] It carries no cutaneous sensory fibres.

It would appear that the 'disappearing thiopentone' extravasated from a vein deep in the posterior fascial compartment, and caused either direct neurotoxicity to, or pressure neuropathy on, the motor branches from the deep branch of the radial nerve supplying extensor pollicis longus and extensor indicis. This regrettable sequel to intravenous thiopentone would appear to be neither predictable nor, under the circumstances, avoidable.

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Assisted ventilation and the Servo ventilator in infants

Dr Bingham and colleagues' article on the laboratory assessment of the Servo ventilator (*Anaesthesia* 1986; **41**: 168–72) was very interesting. We agree with the majority of the article, but we would like to make two points relating to the safety of the continuous positive airway pressure and intermittent mandatory ventilation system as shown in Fig. 1 of the article.

In our intensive care unit we use a very similar external system attached to our Servo 900B ventilators for infants and small children. Our system differs in two minor but important safety features, namely the use of a 5-litre reservoir bag instead of the 2-litre bag shown and the use of a preset pressure release valve placed between the one-way valve and the patient. In the event of occlusion of the expiratory limb, the greater compliance of the 5-litre reservoir bag, together with the blow-off valve, offer better protection to the infant from excessively high airway pressure than does the system described by Dr Bingham *et al.* (in view of the fact that at least 6 litres/minute of gas continues to flow into the system). We accept that the airway pressure upper alarm limit on the Servo 900 models will, if set correctly, give warning of the high airway pressure, but it does not protect the patient, it only warns staff; in the interest of patient safety these minor modifications should be included in the system.

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A reply

Thank you for giving us the opportunity to reply to the above letter. The Servo ventilators do provide some protection against high airway pressure in addition to the alarm during intermittent mandatory ventilation in that the ventilator inspiratory phase is terminated if the preset pressure limit is reached. We agree that this will be ineffective if the expiratory limb is obstructed and do in fact point out in our paper that a pressure release valve is desirable (legend to Fig. 1). We have used a 2-litre reservoir bag in the 3 years the system has been in use (approximately 1500 patients) and have had no problems attributable to excessively high airway pressures.

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Paradoxical air embolus

The article by Clayton *et al.* (Anaesthesia 1985; **40:** 981–9) was most interesting. Their fourth case was similar to one with which I was involved; the patient was a fit 57-year-old male who had a posterior fossa craniotomy in the sitting position for removal of an acoustic neuroma. He had previously had a patent ductus arteriosus closed, but had no other medical history of note.

No premedication was given. Induction of anaesthesia was with sodium thiopentone and suxamethonium, then his trachea was intubated and his lungs ventilated with 66% nitrous oxide in oxygen. Anaesthesia was maintained with alcuronium, fentanyl and droperidol. A central venous line and arterial line were inserted and a Sonicaid Doppler probe was attached to the anterior chest wall over the region of the right atrium.

There was Doppler evidence of an air embolus shortly after the opening of the posterior fossa. The neck was squeezed and an open venous sinus was sealed. The operation then proceeded uneventfully until the packs over the cerebellum were removed, when air was seen in the superficial cerebellar arteries. The nitrous oxide was switched off, the neck squeezed and an open vein sealed. Muscle relaxation was reversed at the end of the procedure with atropine and neostigmine. He was, at this stage, unresponsive to commands, with limb rigidity, pinpoint pupils and periodic breathing. Mechanical ventilation of the lungs was instituted, but his condition gradually deteriorated, and he died one week after the operation.

The interatrial septum was closely examined at post-mortem examination and found to be intact, as was the closure of the ductus arteriosus. The left upper lobe of the lung contained areas of gross fibrosis.

This case demonstrates two points: firstly, that the use of a Doppler probe did not pick up the air embolus at the end of the procedure and, secondly, that a paradoxical air embolus may occur with normal cardiac anatomy. It was postulated in this case that the area of fibrosis in the lung may have provided a route for air to pass from the venous to the arterial circulation.

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A reply

Dr Harrison's interesting case clearly demonstrates that paradoxical embolism is possible without an intracardiac septal defect; a similar case was reported by Marquez in 1981.[1]

It is not always necessary to have abnormal pulmonary pathology and arteriovenous shunts for the transpulmonary passage of air. Butler and Hills[2] have shown that the lung only has a finite capacity to filter air bubbles. Once venous air infusion rates exceeded 0.30 mg/kg/minute arterial spillover occurred. In fact, at infusion rates of 0.35 ml/kg/minute 50% of their dogs demonstrated arterial bubbles.

It seems likely that subclinical paradoxical embolism is occurring far more frequently than we realise.

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Bell's palsy during epidural anaesthesia

A 22-year-old primigravida was admitted for induction of labour at 39 weeks gestation after being found to have a blood pressure of 150/105 mmHg. She had no peripheral oedema or proteinuria, although she had complained of occasional frontal headache over the previous 7 days. There was no significant past medical history and the only other potential obstetric problem was a degree of cephalopelvic disproportion. Her weight was 68 kg.

A lumbar epidural injection was carried out at $L_{2/3}$ interspace without any difficulty and the catheter inserted 3 cm into the epidural space. The block was maintained with 6–8 ml of bupivacaine 0.375% every 2 hours with good control of blood pressure and adequate analgesia. Twelve hours later after failing to progress in second stage the block was extended to T_5 with a further 18 ml of bupivacaine 0.5% for trial of forceps or Caesarean section if necessary. The total dose of bupivacaine over 12 hours was 295 mg.

Keilland's rotation and a midcavity forceps delivery was successfully carried out. However, during this time in theatre she began to complain of numbness on the left side of her face and had developed noticeable dysarthria. On examination there was no extension of the sensory block above T_5 or any sensory block of the face; however, it was apparent that she was developing a left-sided facial weakness which by the end of the procedure was a dense facial palsy involving upper and lower divisions.

There was no improvement over the next few days and the neurologists confirmed the diagnosis of a dense unilateral Bell's palsy. There were no other neurological findings. Electromyography one month later revealed signs of ongoing denervation and therefore a poor prognosis. However, despite the gloomy prognostication she began to recover 3 months later and by 5 months the palsy had completely resolved.

Cranial nerve palsies of all but the first and tenth nerves have been reported with spinal anaesthesia or inadvertent dural tap, but all are extremely rare with the exception of the sixth.[1] Cranial nerve palsies are not a recognised complication of epidural anaesthesia and it is difficult to even postulate any way in which the epidural could be implicated in this case. It is not, however, hard to appreciate the patient's initial concern that the epidural could somehow be to blame, particularly when left with such a disfigurement.

On the other hand, the incidence of Bell's palsy occurring during pregnancy and the immediate puerperium is over three times higher than an equivalent non-pregnant group. The incidence is reported at around 45/100 000 births, 80% of which occur in the third trimester and immediate puerperium, with no apparent relationship to toxaemia, hypertension or primigravidity.[2,3] Suggested contributory factors include alteration in fluid, electrolyte and hormonal balance leading to nerve entrapment or ischaemia, or an increase in *Herpes simplex* infection through gestational immunosuppression. This is an organism often implicated in facial nerve palsy.

Whatever the aetiology of the palsy, the temporal relationship with the epidural was particularly concerning and it was very reassuring to find that the palsy eventually recovered spontaneously, despite the initially poor prognosis.

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Phaeochromocytoma and atracurium

The letter from Dr Sheikh (*Anaesthesia* 1980; **41**: 213–4) describes the satisfactory management of a patient with a phaeochromocytoma using atracurium and labetalol. Dr Sheikh states that atracurium, on theoretical grounds, is the suitable non-depolarising muscle relaxant for use during anaesthesia in these patients. However, atracurium has consistently been shown to cause histamine release, especially when 600 μg/kg or more are used.[1] Histamine is one of the trigger factors for release of catecholamines in patients with phaeochromocytomata and has been used in the diagnosis of these tumours.[2]

Vecuronium, which has failed to show any propensity for histamine release, also offers cardiovascular stability and would appear to offer theoretical advantages over atracurium in this group of patients.

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Marcain shakes

This is a well known, innocuous complication of epidural block, observed most frequently among labouring women and those undergoing Caesarean section. The appelation Marcain is misleading, since the syndrome can arise when local anaesthetics other than bupivacaine are used.

The shaking can start at the beginning, or midway through the period of block and can stop before or at the conclusion of the effectiveness of the epidural. The cause has not yet been determind. Several hypotheses have been presented; the most recent is that it is due to stimulation of thermoreceptors in the spinal canal by the injection of relatively cold solution of local anaesthetic.[1]

We have encountered two cases of unilateral shakes during recent years, one mild and one disturbingly severe. In each case an ipsilateral arm, leg and (probably) trunk was involved; the shaking persisted throughout the period of epidural analgesia provided for labour. The agent used was plain bupivacaine. Both mothers had excellent bilateral analgesia and weakness of both legs. The observations made during labour were emphatically confirmed by the respective mothers during the routine interview on the day following delivery.

I am totally at a loss to explain this phenomenon. Realistic suggestions would be welcomed.

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Reference

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Test doses for epidural analgesia—are we fooling ourselves?

In Dr J.S. Crawford's review article on complications of epidural analgesia for labour (*Anaesthesia* 1985; **40:** 1219–25) it is disturbing to note that in none of the potentially life threatening or moderately serious complications was an appropriate test does used before epidural analgesia was established. A test dose prior to a full dose should forewarn the operator of both intravascular and subarachnoid placement of the epidural catheter. Unfortunately, 2 ml 1% lignocaine does not reliably produce a sensory block when injected into the subarachnoid space, particularly if it is isobaric, nor does it give any guide to intravascular injection.

A reliable test dose of any local anaesthetic should include 15 μg adrenaline which has consistently been shown to cause a tachycardia within one minute of intravenous injection when given with either lignocaine or bupivacaine.[1] For the local anaesthesia component either 0.5% bupivacaine or 1.5% of *hyperbaric* lignocaine may be used. Three millilitres 0.5% isobaric or hyperbaric bupivacaine reliably produces some analgesia within 5 minutes of subarachnoid injection,[2] but little effect is likely to be seen with epidural injection within 2 minutes if injected into the subarachnoid space, but takes a minimum of 4 minutes (mean 9 minutes) to produce any sensory blockage when given into the epidural space.[3]

Unless an epidural test dose contains both an appropriate volume and concentration of local anaesthetic (either 3 ml 0.5% bupivacaine or 2 ml 1.5% *hyperbaric* lignocaine) plus a minimum of 15 μg of adrenaline, it will not warn the operator of inadvertent subarachnoid or intravascular injection. Only if the above criteria are satisfied may an epidural test offer any warning of potential problems.

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efficacy of 1.5% lidocaine with 7.5% dextrose and epinephrine as an epidural test dose for obstetrics. *Anesthesiology* 1986; **64:** 116–9.

A reply

May I point out that the data from which my report was compiled were collected during an 18-year period of clinical observations. During that time, and before it, a multiplicity of test doses have been advocated; these range from the inclusion of 5 mg suxamethonium in the solution (referred to by Massey Dawkins in his comprehensive review,[1]) to the currently strongly supported use of adrenaline. The very fact of this bewildering number of contenders strengthens my conviction that none is truly reliable. No single test has, to my knowledge, been convincingly demonstrated to be infallible within a large series of cases.

The current, and in my opinion admirable advocacy that all therapeutic injections into the epidural space should be in divided doses (for example, 5 + 5 ml for an intended 10 ml top-up) renders the advocacy of a 5 ml test dose somewhat questionable, since the function of one is taken over by the other. One is disinclined to include adrenaline in the injected solution. The plain solution of bupivacaine has a pH value of approximately 6, that of bupivacaine plus adrenaline lies between 3 and 4,[2] and I am reluctant to put such an acidic solution close to naked nerve fibres within the cerebrospinal fluid. Furthermore, a high percentage of patients in obstetric analgesia practice are hypertensive. The prospective of an inadvertent intravenous injection of adrenaline in these women would cause me grave concern. Other practitioners hold contrary views, which I respect, but they are simply another expression of unsubstantiated opinion.

During the period reviewed in my article our test dose has consisted predominantly of 2 ml plain lignocaine, 0.5 or 1.0%. Occasionally a mother will report tingling of her tongue or perioral region, or some dizziness subsequent to this injection; very rarely hypotension has resulted, or a feeling of leg heaviness. The practice is continued, more in obeisance to tradition than for any other reason, although it is my opinion that it is useful to ensure that there is no obstruction to the flow of solution within the catheter and that the latter does not become clogged by the deposition of proteinaceous material whilst dressings are applied.

Doubtless this will offend many of your readers as being a negative attitude. Two things I am positive about: I will never subscribe to the practice of injecting a test dose through the needle and then of inserting the catheter, followed by a formal dose through the latter. Secondly, it is of incomparably greater importance to be able promptly to institute the appropriate resuscitation, should an injection be inadvertently made intravenously or intrathecally, than it is to employ any of the advocated techniques of test dosing.

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Iatrogenic hypotension

Percutaneous catheterisation of the radial artery is a standard procedure for peri-operative intra-arterial blood pressure monitoring of adults undergoing cardiopulmonary bypass surgery.

A patient presented for aortocoronary vein grafting. Intra-arterial monitoring was established using a 20-gauge Argyle medicut cannula inserted into the left radial artery. The patient remained stable during retraction of the sternum and elevation of the pericardium, until immediately prior to aortic cannulation. The systolic blood pressure decreased to 50 mmHg and the arterial waveform developed the characteristics of a damped trace at this time. The monitored blood pressure remained low, despite fluid loading and intravenous calcium chloride. Cardiopulmonary bypass perfusion was established without delay.

The displayed radial artery pressure when bypass was established was 30 mmHg, with a flattened trace, while the aortic line pressure was 180 mmHg. It was felt that the radial artery pressure was inaccurate. The transducer was recalibrated and there was free aspiration of arterial blood from the line; repositioning of the left hand did not affect the waveform and the left hand was clinically well perfused. The aortic pressure, measured directly via a 21-gauge needle and connected to the same transducer, was 60 mmHg and so this pressure was monitored during cardiopulmonary bypass perfusion.

When the graft was in place cardiopulmonary bypass was withdrawn and the circulation was re-established. However, the discrepancy between aortic and radial artery pressures persisted. When the sternal retractor was released, the radial artery pressure tracing returned to normal and the difference disappeared.

Hypotension in the period prior to cardiopulmonary bypass is not uncommon. This may be due to a poorly contracting ventricle, blood loss, lifting of the pericardium or may be consequent upon rhythm disturbances. None of these factors was contributory to the hypotension seen in this patient. However, immediately prior to cannulation, the sternal retraction had been increased. This probably distorted the subclavian artery at the thoracic inlet with the production of a damped, low pressure radial artery recording despite clinically adequate left arm perfusion.

We have seen a similar monitoring problem in two further patients since this one. This is not a common anomaly, but when it occurs it is misleading. Unless the cause of the hypotension is correctly interpreted, the wrong decisions may be made and the wrong treatments instituted.

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Overdose of atracurium

We read with interest the article describing histamine release associated with the use of atracurium during neonatal anaesthesia (*Anaesthesia* 1986; **41:** 178–80). There are an increasing number of reports describing this phenomenon and we wish to describe an extreme case.

A 3-week old female infant who weighed 3.9 kg, previously well, was admitted with a short history of vomiting and, on examination of the chest, basal crepitations. Her general condition deteriorated within 24 hours with a dramatic increase in respiratory rate and increased frequency of apnoeic spells. The chest X ray now showed right lower lobe consolidation. More prolonged apnoeic attacks were associated with bradycardia and arterial blood gas analysis confirmed the deterioration. The baby was admitted to the intensive therapy unit and her lungs were electively ventilated. Twenty-four hours later, after an unsuccessful attempt to wean her, ventilation had to be continued.

The child failed to settle, despite adequate sedation and it was decided to give a muscle relaxant. However, 2 ml of undiluted atracurium was given through a central line instead of 0.2 ml, a dose of more than 5.1 mg/kg. The infant immediately flushed to a deep crimson colour and the systolic blood pressure fell to 28 mmHg from a previously stable pressure of 70–80 mmHg. The pulse rate rose from 140 to 180/minute and inflation of the chest became extremely difficult because of intense bronchospasm. Manual ventilation with 100% oxygen was started and 40 ml of human albumin solution was infused. The position of the tracheal tube was checked by laryngoscopy; there was no evidence of laryngeal oedema. A total of 7 ml of 1:100000 adrenaline was required over the next 45 minutes to keep the systolic blood pressure greater than 50 mmHg. The inflation pressures returned to previous values and the blood pressure remained at 60–70 mmHg without support. The child's condition remained stable with no further treatment. She began to move all four limbs vigorously less than 3 hours later and, after sedation, an atracurium infusion was started.

Two days later, the child was successfully weaned from ventilatory support and returned to the paediatric ward, whence 2 weeks later she was discharged.

It now appears that the early claims that atracurium was free of histamine-releasing action are not justified. This effect appears to be dose-related, with sequelae which vary from mild skin reactions to cardiovascular collapse, bronchospasm and laryngeal oedema. Our patient received more than $ED_{95} \times 30$ as a bolus and although the results were sudden and profound they responded to prompt conventional therapy. We wonder whether the outcome would have been so favourable had the child not been intubated and monitored on an intensive therapy unit.

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Pain on intravenous injection

The letter from Dr Coghill (*Anaesthesia* 1985; **41:** 214–5) describes his technique for the avoidance of pain on injection of etomidate. This technique has reduced the incidence of pain on injection of etomidate to 2%, but I doubt that it will be widely adopted.

It requires alfentanil, droperidol, lignocaine and normal saline in addition to the etomidate itself. Each of these drugs requires to be mixed according to Dr Coghill's recipe. It is not only an expensive anaesthetic, but does also appear to have considerable potential for errors in dosage. One twentieth of an ampoule of droperidol and half an ampoule of alfentanil in one syringe and one ampoule of etomidate with, presumably, 4 ml 1% lignocaine and 6 ml of normal saline in another syringe are required for each patient.

This does appear to be an extreme length to go to in order to be able to use etomidate. It may also be that the advantages of etomidate in day case anaesthesia may be lost amongst the pharmacological actions of the other drugs included in the regimen. Perhaps a different agent might provide rapid safe and painless anaesthesia in considerably less time.

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On the choice of relaxants for use in tetanus

Powles and Ganta (*Anaesthesia* 1985; **40:** 879–81)[1] make an excellent case for the use of vecuronium in the management of tetanus during a 19-day period. However, Aldrete and Hendricks[1] have recently emphasised the considerably increased expense of vecuronium and atracurium over the older non-depolarising agents for lengthy cases.

In view of the extreme autonomic instability present in tetanus we suggest the use of a pancuronium–metocurine mixture.[2] This mixture has been shown to possess excellent properties in terms of blood pressure and heart rate stability,[2] and it should prove more economical for long cases.

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A reply

Thank you for the opportunity of replying to Dr Sosis' letter. Metocurine is not available in the United Kingdom, so I have no experience of its use. According to Lebowtiz *et al.* its cardiovascular properties are similar to those of tubocurarine[1] since it produces variable degrees of histamine release and ganglionic blockade. When combined with pancuronium, a small dose of the mixture, administered to ASA grade 1–2 patients undergoing routine surgical operations, did not cause cardiovascular instability and was readily reversible. Whether or not similar conditions would be produced if the mixture were to be administered over a prolonged period of time to patients with tetanus is a matter of conjecture. It might be agreed that it would be better to use a drug with minimal cardiovascular side effects such as vecuronium instead of a combination of two drugs, both of which produce marked cardiovascular disturbance when used in isolation, however stable the mixture appears to be when given to fit patients.

Vecuronium is appreciably cheaper in the UK (approximately £3.00 for 10 mg) than in the USA[2] ($10 for 10 mg). At the risk of being accused of unfettered profligacy I believe that the cost of a vecuronium infusion (£1.20/hour in our case) is reasonable when judged in the light of the overall expenditure involved in the treatment of a patient in an intensive care unit.

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Perineural morphine for the relief of chronic pain

The treatment of clinical pain in the shoulder and arm due to malignant infiltration in the brachial plexus and root compression due to cervical spondyloses or a spinal tumour constitutes a major clinical problem. It is often not sufficient to administer analgesics orally, subcutaneously or intramuscularly. Peridural morphine may offer some relief, but can be associated with serious complications, especially if the catheter is placed subdurally by accident, or subsequently migrates.[1,2] Recently, we reported the beneficial effect of a small dose of morphine administered as an interscalene brachial plexus block.[3] Having treated another three patients, and two of these more than once, we now have further information about the technical procedure and the suitable volume.

It has been found by the use of contrast medium and X ray that the interscalene space can hold about 40 ml of fluid.[4] In the case reported earlier, only 10 ml isotonic saline containing 5 mg of morphine chloride was used.[3] The duration of the analgesic effect was 36 hours. However, our experience seems to indicate that this period is extended with increased volume and dose. Thus, with 40 ml isotonic saline containing 16 mg morphine chloride it was possible to obtain total painlessness for 21 days. The state of consciousness was not affected. Furthermore, in one of the cases, peridural analgesia had been tried twice without success.

The mechanism of action is still uncertain. It has been suggested that centripetal neuro-axonal transport of morphine could be an explanation. It is well known that neither peridural morphine nor their methods last as long.[5] It is our opinion that the right volume to use should be a volume sufficient to fill the interscalene space and it seems that about 16 mg in 40 ml isotonic saline is suitable. A clinical controlled investigation which compares different doses is required. It is very important that the procedure is correctly performed.

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Complication of central venous cannulation

We would like to report an interesting complication of central venous cannulation which occurred recently. A 5-year-old boy, 22 kg, was admitted to the paediatric ward with a relapse of his acute lymphatic leukaemia following a short history of fever with rigors and general malaise. There was no history of bruising or spontaneous bleeding and he was scheduled for a lumbar puncture, bone marrow sampling and central venous cannulation under general anaesthesia.

His full blood count revealed haemoglobin of 9.5 g/dlitre, leucopaenia and thrombocytopaenia, (platelets 21×10^9/litre. Before the procedures, eight units of platelets were infused as cover; the platelet count improved to 90×10^9/litre. The anaesthetic technique consisted of an induction with 50 mg methohexitone and maintenance with a nitrous oxide and oxygen mixture supplemented with enflurane; the patient breathed spontaneously via a Magill system. The bone marrow sampling and lumbar puncture proceded uneventfully and the patient was tilted head down in readiness for central venous cannulation.

The operator attempted cannulation of the right subclavian vein via the infraclavicular route; on the third attempt the patient developed sinus tachycardia of 160 beats/minute and his breathing became irregular, laboured and sounded moist. The mask was removed from his face to reveal a torrential flow of blood from his mouth and nose. We feared that the bleeding stemmed from the tracheobronchial tree, perhaps as a result of trauma from an over enthusiastic operator!

The patient was turned to the left lateral position, 100% oxygen was administered and the procedure was abandoned. Direct laryngoscopy, however, showed no evidence of bleeding from the laryngeal opening, but a steady flow from the posterior nasal space. The haemorrhage gradually tailed off over the following five minutes and the patient recovered fully without further incident.

We therefore concluded that the patient had developed a spontaneous nose bleed as a consequence of high venous pressures generated by a marked head down tilt (25°) and aggravated by the sinus tachycardia at that time. A qualitative deficiency in platelet function and/or capillary fragility could have been contributing factors. We therefore recommend in patients at risk from spontaneous bleeding, the effect of Trendelenberg tilt should be remembered.

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Multiple cannulation of a single vein

We are dismayed by the enthusiasm of a recent communication to *Anaesthesia*, supporting the use of guidewires to proliferate centrally placed venous cannulae (*Anaesthesia* 1985; **40:** 1243). A study of 42 patients at the Brompton Hospital, carried out in 1983 and based on a similar technique, was terminated because of the unacceptably high complication rate. During this study the internal jugular vein was cannulated in the usual manner,[1] with a 14-gauge 9 cm Teflon cannula (Angiocath-Deseret). Two guidewires were then inserted through the cannula, which was removed. Two further 14-gauge cannulae were then threaded over the guidewires to their central venous location.

Complications arising at the time of cannulation included difficulty threading the cannula along the guidewire, difficulty entering the vein, and continuous blood loss after guidewire insertion. Placement of cannulae over the guidewires did not, in all cases, staunch the haemorrhage, and in two patients blood loss exceeded 200 ml. The second of these two patients lost more than 400 ml as a result of the use of this technique, and this complication was responsible for the cessation of the study.

Other problems with our double guidewire technique included difficulty in advancement of 26 of the 84 catheters; seven of the 26 catheters could not be passed successfully and a second venepuncture was required. Haematoma formation at the site of venepuncture occurred in 19 patients. There were flow problems with

29 of the 77 catheters passed over a guidewire and persistent leakage of blood from the site of the successful double guidewire cannulations occurred in six of 35 patients.

Skowronski and Pearson have previously reported a technique for the insertion of two intravascular catheters via a single skin puncture in critically ill patients. Their technique involved replacing a single 14-gauge Teflon cannula with two 16-gauge silastic catheters. They reported an absence of increased bleeding, sepsis or other complication.[3] They did however, omit to mention the number of patients in which this technique had been used, and the fact that they replaced one 14-gauge cannula with two 16-gauge silastic catheters may have contributed to their better results.

We advise caution in the use of the double guidewire technique. In particular, it should be avoided in the following circumstances: in patients with a raised central venous pressure, in patients with deranged clotting mechanisms or platelet abnormalities, in patients in whom heparinisation is intended and in immunocompromised patients in whom the excessive manipulation of skin and cannula may predispose towards sepsis.

The Turtle technique can be endorsed, with these exclusions when difficulty arises during multiple cannulation of a single vein.

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Tunnelling technique for central venous catheters

We were interested to read of Dr Woodhall and Dr Redman's method of central venous catheter tunnelling (*Anaesthesia* 1986; **41:** 224–5) as, with one small difference, it is identical to our own. We disagree with their use of a suture to close the original skin incision at the site of percutaneous cannulation of the subclavian vein on the grounds that not only may the catheter be either punctured by the suture needle or caught in the suture itself, but there is a risk of subsequent infection due to the presence of suture material near to the catheter.

We advocate the use of a small Steristrip wound closure to oppose the skin edges, which not only removes the potential risks already mentioned, but also obviates the need to remove the occlusive Op-site dressing to take the stitch out a few days later another occasion on which infection may be introduced.

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Positioning of double lumen tubes

We agree with Dr Clapham and Dr Vaughan (*Anaesthesia* 1985; **40:** 1111–4) that the new PVC double lumen tubes (DLT) are easier to pass through the larynx than red rubber tubes, but their comments regarding positioning are a different matter. Contrary to our own clinical experience they found that right-sided DLT were easier to position than left. Our clinical impression has been confirmed by Keating and Benumof,[1] who showed that the length of the adult tracheobronchial tree over which a PVC Bronchocath can be moved and still be correctly positioned (its margin of safety) was 21–29 mm for a left-sided tube whilst only 1 mm for the right. Anatomically this can be explained by the small orifice of the right upper lobe in relation to that of the DLT. The margin of safety is so small that we avoid the use of a right-sided DLT whenever possible and prefer to insert a left-sided tube even for left pneumonectomy, withdrawing the tube into the trachea at the appropriate time.

Difficulty or failure in positioning occurred in 20% of Clapham and Vaughan's patients. We recommend the use of a well lubricated, malleable bougie placed into the correct main stem bronchus under direct vision using a rigid bronchoscope. The DLT can be introduced over the bougie. Should a question ever arise in clinical practice regarding tube position, the convention of unilateral clamping and auscultation for confirmation is unsatisfactory. Correct tube placement should be ascertained by fibreoptic bronchoscopy which should certainly be performed in all clinical research trials.

Finally, we disagree that PVC tubes be used routinely for training registrars and suggest the continuing use of the more difficult red rubber tubes, since the ability to insert these rapidly and with competence can, on occasion, be life saving.[2]

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A reply

The clinical impression that right-sided double lumen tubes (DLT) are more difficult to position than left sided tubes remains an impression. The elegant study by Keating and Benumof[1] compared the measurements of bronchial trees and DLTs and calculated theoretical margins of safety for their positioning; they did not, however, *use* DLTs.

In our prospective study, there was no statistically significant difference ($p > 0.05$) in the time to correct placement of left and right-sided DLTs. It is also interesting that Robertshaw,[2] in his original paper, commented that intubation with a right-sided DLT was even easier than with a left.

We set out to compare the two types of tubes as we would normally use them in clinical practice, using clamping and auscultation, which are well recognised and accepted techniques.[3–5] However, we agree that fibreoptic bronchoscopy could be used in future clinical trials on the positioning of DLTs, provided that they are also used routinely in clinical practice.[6]

We would be interested to know what Dr Rocke and colleagues would advise their trainees to do in the presence of a possible rupture of the left bronchus or of torrential haemorrhage from the left lung. If right-sided tubes are rarely used, then their experience in positioning would be very limited and possibly life threatening. Furthermore, we strongly disagree that registrars should be taught and be expected to use the 'more difficult red rubber tubes', particularly in emergencies. Surely the registrar, and even senior members of staff, should have the best possible chance of success and use PVC DLTs and thus help rescue the patient.

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Radiological contrast media and atrial fibrillation

Intravascular contrast media are essential for diagnostic radiology.[1] Previous generations of high osmolality contrast media were often responsible for serious adverse reactions.[2] The second, newer generation of low osmolality contrast media have been introduced recently[2] and they have substantial advantages over older preparations. Obvious advantages are less cardiac depression, smaller increase in blood volume, lower renal toxicity and a (probable) reduction in adverse reactions.[3] Urografin is still widely used, but is now being replaced by newer contrast media. Many different electrocardiographic changes have been observed following injection of contrast media,[4] which are important for anaesthetic practice. The mechanism of these changes is unclear, but factors such as the introduction of a sudden hyperosmolar volume load, direct myocardial toxicity and neurogenic stimulations have been blamed.[4] We report an unusual case of temporary reversal of atrial fibrillation to sinus rhythm after injection of urografin, in contrast to the production of a dysrhythmia; this has not been reported before.

A 58-year-old man, a smoker who suffered from diabetes, atrial fibrillation and peripheral vascular disease, was scheduled for aortogram under general anaesthesia. His diabetes was controlled by diet and he received digoxin for atrial fibrillation. He did not have any clinical features of heart failure. He was premedicated with papaveretum 15 mg and atropine 0.6 mg intramuscularly one hour before before operation. He was pre-oxygenated with oxygen for 5 minutes. Anaesthesia was induced with thiopentone and intubation was facilitated with suxamethonium. Anaesthesia was maintained with oxygen, nitrous oxide and halothane and he breathed spontaneously through a Bain system in the prone position. The ECG and arterial blood pressure were monitored throughout the procedure. Immediately after the injection of urografin, the atrial fibrillation changed to sinus rhythm, but reversed after 10 minutes. The X ray had to be repeated, due to technical problems; during the second injection of urografin, the atrial fibrillation again changed to sinus rhythm and he remained in sinus rhythm for 3 days.

We do not understand the mechanism for this change, but it was clearly related to the injection of urografin and we wonder if others have similar experience.

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Lanz™ valve—A method of circumventing a leaking valve

The tracheal mucosa becomes ischaemic when the pressure of the tracheal tube cuff exceeds capillary perfusion pressure.[1] To reduce the major complications which result from excessive pressure by the tracheal tube cuff, the use of the Lanz type has been suggested in the intensive therapy unit.[2] Lanz™ valve utilises a principle of automatical regulation of the speed of pressure release from the cuff to a latex balloon (inside the Lanz™ valve); the cuff seal pressure is maintained at a constant pressure below 25 mmHg throughout the period of intubation so that dangerously high pressure cannot be generated by overinflation of the cuff.[3] However, it has been suggested that high-volume, low-pressure cuffs may not produce effective seals.[4]

We have been using a tube designed on the above principle, which is currently being marketed as the Hi-lo/Lanz™ tracheal tube (Mallinckrodt). We have noticed on many occasions that the Lanz™ valve leaks after prolonged use, particularly when there are water droplets in the pilot tube. There is a small component of water vapour which contributes to increase in the volume and pressure of tracheal tube cuff.[5] When this water vapour travels towards the pilot tube, it comes in contact with the lower temperature of the atmosphere and the vapour condenses into water droplets. These droplets somehow affect the performance of the Lanz™ valve. There is no room to apply artery forceps to prevent or lessen leakage. Manufacturers suggest that the valve should not be modified and so imply that the tube needs to be changed every time, even if there is a simple leak in the valve, irrespective of the present circumstances. A balance must be drawn between the risks of changing the tracheal tube and of circumvention of the problem of a leaking valve.

The problem of a leaking valve can be overcome by attaching the male end of a polypropylene one-way valve (Portex part No. 700/322/010) to the injection (female) port of the Lanz™ valve. The cuff is then inflated just to seal in the customary manner for other cuffed tubes.

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Location of the adjustable pressure limiting valve

The article by Dr Puri and Dr Varma (*Anaesthesia* 1985; **40:** 889) was interesting. They describe two systems in which both fresh gas flow and the adjustable pressure limiting (APL) valve lie between the two one-way valves. In their first system (Fig. 1), where they lie together, there is wastage of fresh gas from the APL valve. It is obvious that anything which separated the two would be of benefit.

In their second system, the fresh gas flow is still on the same side of the one-way valves as the APL valve, but separated from it by the sodalime absorber. They claim that retrograde spread of the fresh gas then results in gas, from which CO_2 has been absorbed, being expelled from the APL valve. This is wasteful. It was disappointing that no experimental evidence was included to support their contention and I therefore decided to investigate this.

An Oxford ventilator (Fig. 2) replaced the patient, to

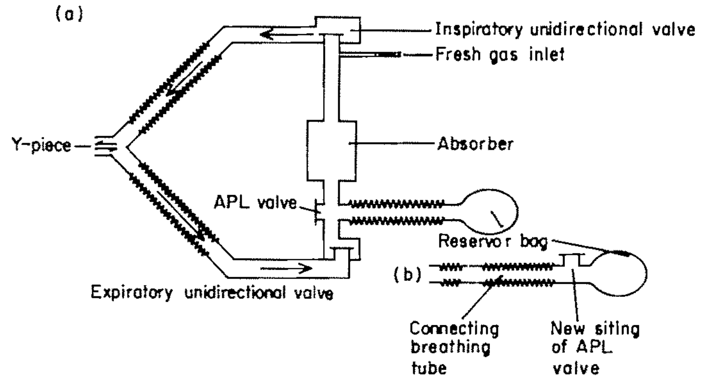
(a)
Inspiratory unidirectional valve
Fresh gas inlet
Y-piece
Absorber
APL valve
Reservoir bag
Expiratory unidirectional valve
(b)
Connecting breathing tube
New siting of APL valve

Fig. 1.

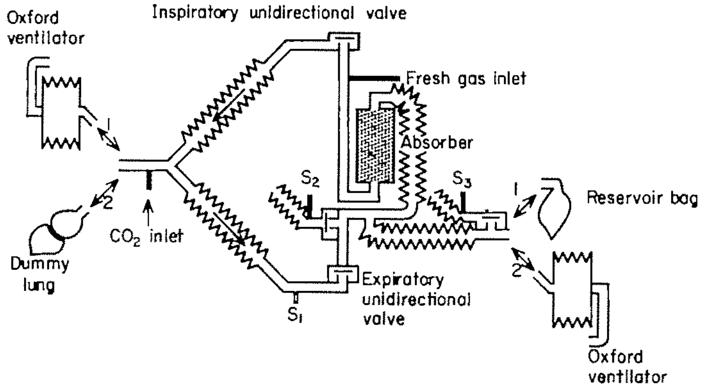

Fig. 2. System used to test the theoretical lay-out of Fig. 1. Position 1 alternative for simulated spontaneous ventilation; position 2 alternative for IPPV. Sample sites (▮) CO_2 analysis. S_1, expiratory limb; S_2, exit from original APL valve; S_3 exit from new APL valve site.

simulate spontaneous respiration. It inspired from the patient's Y-piece and expired into it. For intermittent positive pressure ventilation the ventilator was used to drive the circle which ventilated a dummy lung. For both spontaneous ventilation and IPPV the fresh gas flow was 2.5 litre/minute oxygen. Carbon dioxide was added at 250 ml/minute to the inspiratory side of the lung through a T-piece. The respiratory rate was 20/minute. Tidal volumes of 200, 400 and 800 ml were used. Carbon dioxide concentrations were measured using a Gould infrared absorption capnograph. Samples were taken from the expiratory limb of the circle, of the gases expired through the APL valve in the traditional position in the circle and thirdly of the gases spilling through the APL valve in the new position.

The carbon dioxide concentration decreased, as would be expected, from 2.3% when the tidal volume was 200 ml, to 1.6% at 400 ml and 1.2% at 800 ml. There was, however, no difference in the concentrations from any of the three sites and this was not affected by a change in the mode of ventilation. Waste of purified gas would be expected to dilute the CO_2 concentration.

No benefit from the new location of the valve, within the limits of the flows which were used, was demonstrated. The Blease circle system included a 55-cm anaesthetic hose, from the APL valve to the inlet of the carbon dioxide absorber (this is also true of other circle systems). This tubing had a dead space of 270 ml. The retrograde flow described by Dr Puri and Dr Varma, which might have been expected to expel gas from the absorber through the APL valve, never actually reaches further than the anaesthetic hose, which would explain the failure to produce the predicted improvement. My experiments do not suggest that their position is worse than the original, but simply that it does not confer any benefit.

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A reply

Thank you for the opportunity to reply to Dr James; we are grateful to him for his comments. We do not fully understand the experimental design which Dr James has used. It is now agreed that the most appropriate position for an APL valve is on the Y-piece in spontaneous ventilation[1,2] and our article only concerned controlled ventilation. It is not clear how the APL valve on his circle system was managed during controlled ventilation while the tidal volume was kept constant. The new location for the APL valve (Fig. 1b in our article) prevents exodus of CO_2 free gases only if the volume between the canister and the original location of the APL valve is less than the volume of fresh gas coming into the system during expiration and during the expiratory pause of one respiratory cycle.

If the respiratory rate is 20 breaths/minute and the fresh gas flow is 2.5 litres/minute, an inflow of about 93 ml fresh gas occurs during expiration and the expiratory pause (assuming that the inspiratory time is one second). This small flow is insufficient to push a volume of 270 ml of CO_2-free gas all the way to the APL valve. When the fresh gas flow is 3 litres/minute and the respiratory rate 14 breaths/minute, with an inspiratory: expiratory ratio of 1:2, retrograde flow of about 142 ml occurs. If the volume between the APL valve and the canister is less than 142 ml then moving the APL valve (as in Fig. 1b) will be advantageous. These estimates assume that plug flow takes place, but the calculation is more complex if flow is cone-fronted.

The intention of the new location is to increase the distance between canister and the site of escape of gases. Any other arrangement serves the same purpose. The Heidbrink valve is available on most machines and can be both attached and manipulated easily for manual ventilation.

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Minitrach in airway obstruction

We should like to report a method of managing a worrying problem using a device which has only recently become widely available. A 22-year-old male sustained a compound fracture of the mandible. Some soft tissue trauma made tracheal intubation difficult, but a 7.0 mm Mallinckrodt preformed nasal tube was successfully inserted. Surgery was performed, but because of increasing swelling the tube was left in place and the patient transferred to the intensive care unit. Mechanical ventilation of the lungs was considered desirable in view of the small diameter of the tube.

Difficulties with tracheal toilet (due to the shape and size of the tube) forced us to remove the tracheal tube after 36 hours, somewhat earlier than we would have preferred. The integrity of the upper airway was still in doubt, so it was decided to perform cricothyroid intubation with a Portex 'Minitrach' to provide an easy portal of entry for a 16-gauge cannula driven by a Sanders injector; this was performed easily under local anaesthesia.

The patient was able to maintain his own airway after extubation and the Minitrach was removed after 24 hours. The patient was later asked to close his mouth and pinch his nose and breath through the 4.00 mm id cannula of the 'Minitrach', which he tolerated comfortably for some minutes. Surgery was required some days later and the surgeons were able to perform a conventional tracheostomy under local anaesthetic with no problems from the previous tracheal cannulation.

We cannot find any mention of the use of the Minitrach system in this way and our experience shows that this simple system provides an adequate airway in the short term in a case of upper airway obstruction.

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The Haemonetic cell saver

Jehovah's Witnesses (JW) who present for major surgery continue to pose a challenge to anaesthetists. Refusal to accept blood transfusion during an emergency can lead to death from exsanguination.[1] Intra-operative autotransfusion and cell salvage have been used extensively in major vascular surgery and trauma.[2]

This is a case in which a Haemonetic cell saver® was used in a JW undergoing major vascular surgery. A 46-year-old female JW presented for elective aorto-bifemoral reconstruction. It was established at the pre-operative visit that the patient was willing to accept the technique of intra-operative blood salvage and the use of Haemonetic cell saver.®

The cell saver was used to salvage the blood which was lost in the wound. Thus, 1200 ml of blood was collected during surgery in the reservoir of the cell saver and, after washing, 950 ml was returned to the patient. She also received 1000 ml of normal saline and 200 ml of 20% mannitol. The blood pressure and pulse rate remained stable throughout the surgery.

Haemonetic cell saver® is a small portable centrifuge, with which blood is collected into a cardiotomy reservoir by means of vacuum aspiration; intravenous heparin 5000 is added as an anticoagulant. The intact red cells are separated by centrifuge while the plasma, which contains haemolysed cells, cell stroma, heparin and electrolytes is eliminated separately. When the concentration of red cells reaches a haematocrit of 55–65%, the contents of the centrifuge bowl undergo a dilutional type of wash until the effluent from the bowl has been cleared of haemolysed cells. Finally, the washed red cells are pumped into a blood bag containing no anticoagulant, and are returned to the patient at a 55–65% haematocrit value.

Autotransfusion is a term applied to any method which returns blood to the same person from whom it was collected. Two methods are possible: preoperative collection and storage, enhanced by current methods of freezing allows for longer storage, but this process is expensive and unacceptable to JW's; intraoperative blood collection and replacement with clear fluids initially, followed by re-administration at the end of the procedure.

Coagulation is a major problem associated with autotransfusion; some patients develop generalised oozing, which is unresponsive to fresh frozen plasma and platelets.[3] Thrombocytopaenia has also been reported, which is related to the removal of platelets by blood filters.

A major disadvantage of autotransfusion is the complications which result from either particulate or air emboli; however, the advantages are blood compatibility, fewer transfusion reactions and reduction in blood wastage.

Some JW patients agree to autotransfusion techniques, despite their refusal to accept blood products, so it is possible to use this device to perform surgery involving excessive blood loss and which would otherwise have been too dangerous to undertake.

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Armoured tracheal tubes for neuroanaesthesia

We would like to rise to Dr P.J. Wright's challenge in his letter (*Anaesthesia* 1986; **41:** 213).

Recently, a middle-aged man whose trachea had been intubated with a plastic nasotracheal tube for 24 hours came to surgery for cerebellar decompression. The prone position was chosen and one of us (P.E.M.) made the decision not to change the tube to an armoured one. It is normal practice in this unit to use armoured tubes, but in this case it was mistakenly thought that a nasotracheal tube was unlikely to kink as the radius of curvature of a nasotracheal tube is greater than that of an oral tube. Prior to surgery the surgeon flexed the patient's neck and it became impossible to ventilate the patient. Tube kinking was suspected. When the neck was deflexed the patient was easy to ventilate. The tube was replaced with an oral, armoured latex tube and positioning and surgery proceeded uneventfully.

A variety of postures are employed in neurosurgery, ranging from those where tube kinking is unlikely (for example during a frontal craniotomy in which the patient's head is in neutral rotation and the neck relatively unflexed), to positions where the risk of kinking the tube is high (for example where a more posterolateral approach is required, which necessitates flexing and rotating the neck).

Two special cases exist. Firstly, there is the sitting position for an approach to the posterior fossa; this often demands extreme neck flexion, which can lead to kinking of an unarmoured tube. Secondly, there is the prone position, either for an approach to the posterior fossa or for operations on the back. Here the patient's head may be supported in a headrest or caliper, when conditions similar to those in the sitting position apply.

We have personal experience of kinking of oral plastic tubes in the neurosurgical intensive care unit and consider that an oral armoured tracheal tube may be desirable for prolonged intubations if for any reason the nasotracheal route is not available for a plastic tube.

During a major craniotomy a tracheal tube, once inserted, cannot easily be changed. Hence, loss of the airway can be potentially disastrous. We agree with Dr Wright that plastic tubes become quite malleable at body temperature, but suggest that it is this very quality which allows the tube to kink gradually in the course of an anaesthetic so that airway obstruction occurs at a time when it is least possible to deal with promptly and adequately. The admitted advantages of plastic tubes are not sufficient to outweigh this risk. We suggest that the clinical trial that Dr Wright suggests has already been done over the years and it is that experience on which the present policy of using armoured tubes is based.

Finally, we consider that there would not be a viable defence in a court of law, were the kinking of a plastic tube to be implicated in the death of a patient during a neurosurgical procedure.

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May I add to the discussion on the need for armoured tracheal tubes for neuroanaesthesia (*Anaesthesia* 1986; **41:** 213)? At the University of Texas Health Science Center in Dallas, three cases of hoarseness associated with vocal cord paresis were noted postoperatively in patients who had been intubated with armoured tracheal tubes for neuroanaesthetic procedures. It was considered that the use of rigid armoured tubes for prolonged procedures, often combined with considerable neck flexion or extension, might have been responsible. It was decided to use Sheridan high volume cuff tracheal tubes for all neurosurgical procedures.

Over 350 neurosurgical procedures were subsequently performed without complication. In particular, no further instances of vocal cord damage were noted. These findings not only support the suggestion that neurosurgical cases may be successfully managed without the use of armoured tracheal tubes, but also that the use of armoured tubes in such cases may lead to an increase in morbidity.

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Dr P.J. Wright (*Anaesthesia* 1986; **41:** 213), questions the need for the use of the tracheal armoured tracheal tube in neurosurgical cases. This practice developed because the only alternative tubes available were the standard red rubber ones which, of course, are famous for their kinking properties. Nowadays, we have a wider selection of tubes and although I prefer armoured tracheal tubes, the new disposable implant tested tubes, are acceptable if the patient is in the supine position. However, in paediatric neuroanaesthesia, I always use armoured tubes since the small diameter nonarmoured tubes can kink in any position.

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In vitro buffering capacity of Alka Seltzer Effervescent

Dr Murrell and Professor Rosen (*Anaesthesia* 1986; **41:** 138–42) have pointed out the serious problems with magnesium trisilicate mixture B.P.C. and also the drawbacks of the standard 0.3 M solution of sodium citrate; these are a short storage life and palatability. They have attempted to solve these problems using a proprietary preparation Alka Seltzer Effervescent, which contains sodium bicarbonate, potassium bicarbonate and citric acid.

There is, however, a commercial preparation of sodium citrate, Cymalon (Sterling Health), which has a 4-year shelf life and which is pleasantly flavoured. It comes in convenient sachets and is intended for use in the symptomatic treatment of cystitis. We have used this preparation in the Vale of Leven District General Hospital for over a year and it has gained acceptance by both staff and patients. If one sachet containing 7g of powder, which is equivalent to 4 g of sodium citrate Ph. Eur., is dissolved in 40 ml of water a 0.34 M solution results. Our regimen for emergency Caesarean section is to administer 200 g of cimetidine intramuscularly as soon as the decision is made to intervene operatively and then 30 ml of this mixture is administered in the anaesthetic room immediately before taking the patient into theatre and inducing anaesthesia. A small sample of 17 patients had their stomachs aspirated after delivery; the resultant pHs were in range 4.2–6.5 (mean 5.74) and the volumes were between 4–240 ml (mean 75.5). This is too small a number of patients to state more than that it was apparently effective in this small group.

Table 1. *In vitro* testing of 30 ml each of standard 0.3 M sodium citrate and Cymalon 7 g diluted in 40 ml water

	Sodium citrate 8.8 g% W/V (0.3 M)	Cymalon 7g in 40 ml water (0.34 M)
Initial pH	8.50	5.95
The volume of 0.1 M HCL added to 30 ml of each solution to reach the pH values below		
pH 3.0	202	198
pH 1.2	342	338

In vitro testing showed an almost identical titration curve to 0.3 M sodium citrate, as would be expected. The results are given in the table. The disadvantage of making up 40 ml then discarding 10 ml would be solved if the manufacturer's would make available a 5.25 g sachet which one could add directly to 30 ml water. A reduction in the flavouring would also be helpful. A warning on the sachet against its use in pregnancy refers to its *repeated* use during pregnancy and is equally true of sodium citrate solution. The dose, as above, contains less than one eighth of the amount of sodium contained in the 2 litres of Hartmann's solution commonly given during epidural anaesthesia for Caesarean section.

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Distortion by sterilisation

There has been an increasing trend towards disposable plastic equipment in anaesthesia and this has caused some unexpected problems. Figure 1 shows a new Ohmeda 'Series 15' tracheal tube connector and a separate connector which has been autoclaved four times, as recommended by the manufacturer and which is grossly deformed. (Particular care was taken to avoid any weight or pressure on the connectors during sterilisation.)

The manufacturers are aware of this matter and the items have been taken off the market; however, they are still readily available. The problem is that the deformity starts to occur after the first sterilisation and although minor at that time, eventually the connexion between the catheter mount and tracheal tube cannot be made. This could lead to unexpected and potentially dangerous problems, since a slight deformity may not be recognised and may result in unexpected need to replace a tracheal tube.

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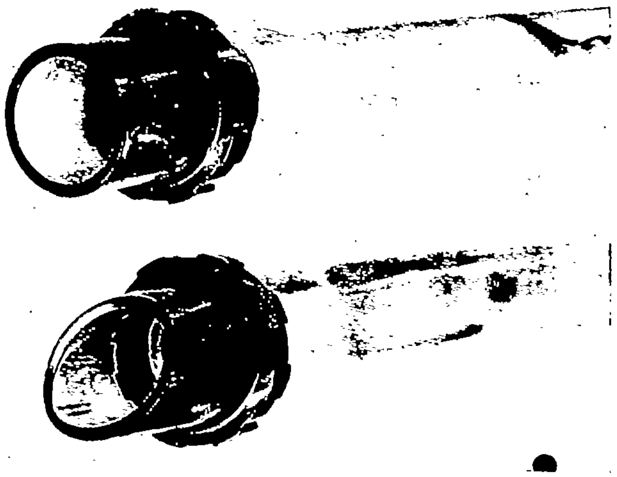

Fig. 1.

High halothane concentrations from reversed flow in a vaporizer

We refer to the letter from Dr Railton and Dr Inglis (*Anaesthesia*, 1986; **41**: 672). We are very concerned that an incident of this nature was reported one month after the servicing of the switch on the Selectatec back bar.

Our Service Department is fully aware of the procedures and checks which are implemented in the case of these older versions of the Selectatec. Their importance has been re-emphasised following the report. All such equipment serviced by our engineer has been checked and found to be operating correctly.

We note the author's recommendations which are in line with our own thinking that changeover switches should be avoided and the current versions of Selectatec do not include a switch. A programme for part-exchanging Selectatecs of this older type with the latest version as appropriate is in the course of preparation.

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Peri-operative fluid administration

The article by Dr Twigley and Dr Hillman (*Anaesthesia* 1985; **40**: 860–71) on the use of colloid solutions intra- and peri-operatively argued the case well for more frequent employment of these solutions. In particular, few would now disagree with the irrationality of the use of crystalloids in the treatment of hypotension associated with epidural anaesthesia. However, in defence of crystalloid administration, some points should be appreciated.

It has been shown that the use of glucose-containing solutions during abdominal surgery leads to a more favourable metabolic profile in respect of glucose and insulin levels measured intra-operatively.[1] The intracellular use of glucose as a result will be enhanced and the rise in anabolic hormone may result in beneficial reductions in protein catabolism. Furthermore, the patient's normal fluid requirements should be provided as a background against which intra-operative losses are superimposed.

Recent experience has shown that enthusiastic pre-operative bowel preparation, and in particular where oral mannitol is employed, may result in considerable degrees of dehydration in patients who present for abdominal surgery.[2] In these patients, induction of anaesthesia may result in a profound fall in blood pressure as a consequence of the depletion of extracellular volume. This depletion of extracellular fluid is appropriately replaced with isotonic solutions of crystalloids.

For these reasons we must be guarded in our approach to peri-operative fluid replacement and we must not be too ready to abandon the use of crystalloids in favour of expansion of the intravascular space in isolation.

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A reply

Thank you for the opportunity to comment on this letter. It appears as if the author favours the use of glucose-containing solutions intra-operatively on metabolic grounds. One could not argue against the theoretical basis for such a suggestion but, in practical terms, most routine surgery does not require parenteral nutrition of any kind.

The glibness of the suggestion that a patient is given 'normal fluid requirements ... as a background against which intra-operative losses are superimposed' demands closer scrutiny. What are normal requirements and losses; can the body adequately compensate in the short term; would this compensation stretch the patient's reserves; does fluid replacement affect the compensatory process? The theme of my article is that the normal fluid requirements have been grossly over estimated, that overinfusion of fluids can cause complications, that the body can adequately compensate, in the short term, for most elective surgery, and that fluids probably do not affect that compensatory process anyway. The isolated problem of pre-operative bowel preparation with oral mannitol can cause problems. Mannitol causes depletion of both the intracellular and extracellular volume. The profound decrease in blood pressure on induction of anaesthesia is as a result of intravascular depletion. Isotonic solutions of crystalloids would neither adequately replace the total body water, nor efficiently protect against hypotension. A more logical approach would be to replace the water losses with hypotonic saline and resuscitate the intravascular space with colloid. This would adequately rehydrate the patient as well as preventing the profound fall in blood pressure. An even better suggestion may be to talk to the surgeons and stop the dangerous practice altogether.

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Microfiltration of blood

Recently, Mollah and Bradshaw compared a new blood microfilter, the Swank 6000-4 to three other blood microfilters (*Anaesthesia* 1984; **39**: 1018–22). Pooled blood, 29.75 days old, was infused at 300 mmHg pres-

Table 1. Mean flow rates in ml/second for 250 ml of blood (Mollah and Bradshaw) or packed cells (Cullen) infused at 300 mmHg (SE)

	Pall		Fenwal		Swank		Intercept	
Filter	Mollah	Cullen	Mollah	Cullen	Mollah	Cullen	Mollah	Cullen
Unit	12.42	2.12	12.33	3.4	12.038	2.63	12.24	3.73
no. 1	(0.214)	(0.174)	0.176)	(0.855)	(0.141)	(0.66)	(0.185)	(0.190)
Unit	11.47	1.99	11.035	2.4	10.8	0.819	11.06	2.53
no. 2	(0.363)	(0.285)	(0.273)	(0.285)	(0.308)	(0.13)	(0.274)	(0.395)
Unit	11.5	1.83	11.197	1.96	10.97	0.89	10.966	1.47
no. 3	(0.325)	(0.316)	(0.195)	(0.316)	(0.157)	(0.18)	(0.309)	(0.475)
Unit	10.31	1.53	10.55	1.31	9.403	0.59	9.66	0.36
no. 4	(0.491)	(0.316)	(0.406)	(0.538)	(0.395)	(0.13)	(0.358)	(0.174)

sure through the various filters in 250 ml aliquots and the flow rate (ml/second) was measured. They described incredibly high flow rates for all four filters, including the new Swank filter as well as the Johnson and Johnson Intercept, the Fenwal 4C 2423 and the Pall SQ 40S, 10 to 12 ml/second or 600–720 ml/minute.

We had previously reported flow rate results with the three older microfilters referred to by the authors, yet our results using type specific packed cells approximately six weeks of age infused at 300 mmHg through the filters were very different (Table 1). Not only were our flow rates for the first 250 ml 22% of those reported by Mollah and Bradshaw, but there was profound diminution in flow rate as the second or third 250 ml aliquot was infused, such that we could only pass 0.59 ml/second of packed cells through the Swank filter by the fourth aliquot. For this reason, we chose not to study the Swank filter further. Because the Fenwal filter and the Bentley filter (not studied by Mollah and Bradshaw) allowed satisfactory flow rates, those filters were studied in more detail.[1]

We used packed cells which were approximately 2 weeks older than the whole blood used by Mollah, but our blood was infused at the same pressure and volume. We did not prime the filter as did Mollah and Bradshaw, but had we done so, our flow rates would have diminished even more quickly. Thus, we must comment that the authors' conclusion, that there was no difference in flow rate through each type of microfilter, applies only to outdated whole blood, not to outdated packed cells, which are almost exclusively used in the United States for transfusion purposes. Furthermore, how did the authors achieve such high flow rates throughout? We agree with the author's screen filtration pressure results demonstrating that the Pall microfilter was less effective in restoring screen filtration pressure to normal than other depth filters.

We call this information to Mollah and Bradshaw's attention because their results with the Swank filter obtained by similar methodology, except for the use of packed cells instead of whole blood, are so markedly different from our own. Blood microfilters must allow rapid infusion rates for massive transfusion to be clinically useful.

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Reference

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A reply

We suggest that the method used in the American study explains the discrepancy between their flow rates and ours. They used packed cells whereas the previous study used whole blood. The viscosity of packed cells is greater than that of whole blood. To quantify this we examined seven samples of packed cells and six samples of whole blood in the Coulter counter and measured their respective whole blood viscosities using a microviscometer (Wells-Brookfield). The results are presented in the following table.

	Packed cells Mean (SEM)	Whole blood Mean (SEM)
Hg g/dlitre	22.4 (1.53)	12.7 (0.36)
Hct	0.693 (0.05)	0.38 (0.01)
Comparative viscosity, centipoise	13.4 (3.55)	4.00 (0.221)

Since flow is inversely proportioned to viscosity,[1] the more than three-fold increase in the viscosity of packed cells as compared to whole blood must obviously reduce the flow rate through any filter.

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Reference

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Difficulties with isoflurane at induction

We were surprised to read that S.M. Short *et al.* (*Anaesthesia* 1985; **40:** 1160–64) had such difficulty with a methohexitone, isoflurane, oxygen technique. In two similar studies that we have recently completed on anaesthesia for outpatient urological procedures, 30 patients received methohexitone, isoflurane, oxygen, 15 received methohexitone, halothane, oxygen and 15, isoflurane, oxygen alone. The principal differences in technique were that we used only 1 mg/kg of methohexitone and also that we used a circle absorber system with a Goldman vaporizer in the system. The incidence of side effects at induction is shown in Table 1. No patient required tracheal intubation and the incidence of coughing associated with isoflurane was much less than that found by Short *et al.*

We would also question their assumption that the substitution of halothane for isoflurane would improve smoothness of anaesthesia. We found no evidence to support this when we compared methohexitone, halothane, oxygen with methohexitone, isoflurane, oxygen; in fact we found the converse, in that, with the exception of excessive salivation, the incidence of side effects on induction was approximately doubled in the halothane group.

We hope to publish the full results of our two studies shortly.

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Table 1. Incidence of adverse side effects during induction, n(%)

Technique	n	Coughing	Excitation	Excessive salivation	Breath holding
Methohexitone, isoflurane O_2	30	7 (23)	3 (13)	12 (40)	1 (3)
Methohexitone, halothane O_2	15	7 (47)	4 (27)	0	2 (13)
Isoflurane O_2	15	3 (20)	5 (33)	1 (7)	1 (7)
Total	60	17 (28)	13 (22)	11 (18)	4 (7)

Radial artery blood flow after puncture

The paper by Dr Wilkins (*Anaesthesia*, 1985; **40:** 896–9) was very interesting. This letter is a supplementary report with an additional observation. The aim of the study was to determine any subclinical change of the blood flow in the radial artery after uncomplicated puncture of the artery in seven patients. No patient had arteriosclerotic disease and all had a normal blood pressure when the puncture was made.

The blood flow in the radial artery was measured in both hands using an ultrasonic technique. Arterial puncture was then made in one wrist. The artery was compressed afterwards for 5 minutes. Fifteen minutes after the puncture the blood flow was measured again. The measurement is semiquantitative (maximum amplitude is recorded in mm); Wilcoxon's test for pair differences was used.

The investigation showed that there were no changes in the arterial blood flow 15 minutes after arterial puncture.

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Thermal injury to the respiratory tract

Dr H.S. Smith and Dr R. Allen (*Anaesthesia* 1986; **41:** 215–6) should be congratulated for identification of a potential problem when two good pieces of equipment are used together. Their fears that thermal injury to the respiratory tract might be caused by hot humidified air are reasonable and have been voiced with regard to children.[1] However, I think that the likelihood of serious or permanent damage is remote.

It is remarkably difficult to cause heat damage to the trachea and bronchi[2] because the airways have a large vascular supply which transfers heat rapidly away. The hand, which has a much poorer blood supply, is much less tolerant of heat. Provided that the larynx is bypassed,[3] the trachea can tolerate dry heat up to 350 C and a review of many experimental reports[4] shows that it requires steam at 94–104 C to produce consistent thermal damage to the air passages. As a personal observation, a peak temperature of 57 C, repeatedly recorded in the oropharynx while breathing heated humidified gas, was found to be uncomfortable but tolerable over a period of several minutes, although this temperature could not be tolerated on the lips.[5] Even when the thermostat of a humidifier was deliberately set at 80 C, with the inspiratory tubing lagged to prevent heat loss between the humidifier and the patient[6] and the hypothermic patient ventilated at this setting for several hours, there was only mild reversible laryngeal oedema and mild tracheal scalding, which was also reversible.[7] In another case,[7] because of failure of a thermometer, a child was ventilated for an unspecified period, probably at least an hour, with hot moist gas at what must have been well over 45 C, there was tracheal haemorrhage and tracheobronchitis but, nonetheless, the child recovered completely. In experiments with dogs, exposure to a sauna at 85 C for 10 minutes daily for 60 days only produced minor reversible changes and only in the trachea and main bronchi.[8]

If airway warming is used to treat accidental hypothermia, it is now recommended that the temperature of the inspired gas should not exceed 45 C because of the risk of damage to the facial skin.[2,5] In animal and clinical work, using 45 C humidified gas for rewarming there has been no evidence of damage to the larynx or trachea.[2] In the problem discussed by Dr Smith and Dr Allen, the patient's trachea was intubated and a gas temperature over 45 C for only 3 minutes at a time is very unlikely to be harmful to the patient. Despite these comments I agree with Drs Smith and Allen that, if the desired effect can be achieved with condenser humidifiers, they should be preferred to heated humidifiers. One reason is that under certain circumstances a heated humidifier may cause the patient to become hyperthermic.[2]

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Postoperative vomiting

Your editorial and article on transdermal hyoscine and postoperative vomiting (*Anaesthesia* 1986; **41:** 1–3 and 16–20) were so much at variance with my daily experience that I had to reach for my pen. When I read that 68% patients had severe nausea and vomiting after major gynaecological surgery and that distressing effects may occur after only minor surgical procedures I felt ill myself.

These days not even 5% feel sick after minor surgery. To reinforce my memory of major cases I retrieved a bunch of case records which included 14 consecutive hysterectomies: six (43%) had no nausea or vomiting, judged by nursing notes, another six (43%) suffered some nausea at times and only one (7%) was distressed with persistent nausea and vomited several times. Intravenous electrolyte solutions were given for about 24 hours (range 18–48 hours) to maintain fluid intake.

Thirty years' practice in anaesthesia makes me confident that my small series could be expanded with similar results; my reputation would not have survived this time if 68% of my major cases had suffered distress. However, without clinical research assistance the large amount of accumulated data cannot be examined in depth and marshalled to support my contention.

The cause of postoperative nausea and vomiting is multifactorial, but it seems clear to me that pain-related sensation plays a large part; when extradural blockade is wearing off some patients experience nausea before pain and a top-up relieves the sickness. Prevention is more effective than an attempted cure and the main failures today are in the provision of adequate analgesia at all times (especially at awaking) and the full use of anticholinergic drugs; glycopyrronium is an essential factor in my success.

Finally, personal attention and care will avoid distress even when nausea and vomiting are tiresome. Good nursing is so important, not just to offer antiemetic drugs but to provide emotional support, frequent mouthwashes and antacids; understaffing or inexperience prolong the agony!

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A reply

Thank you for the opportunity of reply to Dr Gardiner.

We too were surprised at the high incidence of postoperative nausea and vomiting in our series of patients, although we had chosen to investigate this group undergoing major gynaecological surgery because of its known high incidence of this problem. We are certainly not proud of the high incidence of emetic sequelae, even in those patients who were treated with the active drug, and suspect that despite Dr Gardiner's apparent reputation for prevention of these adverse effects, he too cannot be proud of only six of eighteen patients (43%) in his small anecdotal series being free from such effects.

Dr Gardiner's report further illustrates the fallibility of relying on nurses' charts for information rather than careful, repeated postoperative visits by the anaesthetist. It is likely that he would also have found that patients who vomited would not be given anti-emetic drugs and thus not be recorded as suffering from nausea or vomiting. He may also have found that, despite recording the presence of nausea or vomiting, nurses are still reluctant to dispense anti-emetic or appropriate analgesic drugs.

Dr Gardiner's report highlights the problem of postoperative nausea and vomiting and lends support to the hope that our article will stimulate interest in this problem and perhaps lead to more attempts both to record and prevent these distressing adverse effects.

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C.E. BLOGG
J. UPPINGTON

Nausea and vomiting

The article on anaesthesia for extracorporeal shock wave lithotripsy by M.A. Abbott *et al.* (*Anaesthesia* 1985; **40:** 1065–72) clearly states the preference of the authors for an epidural technique of anaesthesia. The discussion of the paper gives very sensible explanations for the differences between the two forms of anaesthesia except for one item: nausea and vomiting.

Nausea and vomiting should no longer be an obligatory side effect of general anaesthesia in 15.3 or 16.1% of cases, as found by the authors and by Gold.[1] The vey reason why 15.3% of patients having a general anaesthetic present nausea and, or vomiting is because they did not receive an anti-emetic either in the premedication, or when narcotics were given per- or postoperatively.

These percentages seem to me unacceptably high in these medically and pharmacologically highly advanced 1980s! Very small doses of powerful anti-emetics (like droperidol) will easily do the job, without side effects of their own. Let us guide our patients safely, but also comfortably through their anaesthetic: *in somno securitas et commoditas!*

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G. VERHEECKE

Reference

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Intradermal testing

The paper by McDonald and Emery on intradermal testing (*Anaesthesia* 1985; **40:** 549–51) contains some aspects which appear inaccurate. The opening statement on the incidence of reactions, for example, is not supported by either of the references cited. Furthermore, the paper from our unit cited in support of the statement that patients with a very high or low plasma IgE level 'may be more prone to reactions' shows, in fact, that IgE level is a poor predictor of likelihood of a reaction.[1]

The paper describes intradermal testing results after a reaction to anaesthesia using a protocol developed in this unit,[2] and concludes from the results that skin tests must be interpreted with caution. The conclusion is correct, irrespective of the fact that the protocol is not followed, in terms of controls, dilutions or timing. The unusual finding in the testing carried out is a number of false positives occurring at high dilutions. We have seen similar results in one patient, but not to as many drugs and, in addition, the positive test were absent at stronger concentrations in our patient. The reason is not known for this phenomenon, but a plausible explanation in the case cited is the volume of injected (stated in error in our (1979) paper protocol to be 0.1 ml).[3] Slavin[4] states that the optimum volume for an intradermal test is 0.02 ml and larger volumes produce false positives; in our experience, injection of 0.1 ml of anything intradermally gives a physical response resembling a wheal.

My concern is that the value of this method of diagnosis of severe reactions resembling anaphylaxis in relationship to anaesthesia, which has been established in several large series,[3,5–9] may be relegated due to this anecdote. In all the large series cited the method did not provide the answer in all cases. It would be extremely surprising if it did and variables, such as the population studied, histamine releasing drugs, variable patient response to histamine release and released histamine, the nonheterogeneity of mast cell populations and the possibility of multiple mechanisms for clinically indistinguishable symptoms make it unlikely that any single test will always be useful.

Our experience of using this technique in over 400 patients to provide reliable guidelines for safe subsequent anaesthesia has not diminished our enthusiasm and refinements on technique, such as those of Galletly and Trueren,[10] may improve its reliability. I am still not aware of any case in the literature where a reaction occurred after multiple drugs and any test, other than an intradermal test, has determined the drug responsible.

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New Lack system tubing

New tubing has been produced for the Lack anaesthetic breathing system which completely eliminates the principal disadvantage of stiffness (*Anaesthesia,* 1985; **40:** 1236–7). It is much lighter and more comfortable to use. Outer and inner tubes are replaced by stronger and more flexible material and the combined weight is reduced from 470 to 320 g. The inspiratory limb volume measures approximately 500 ml, the same as the nominal volume of a Magill attachment. The expiratory pathway resistance of 0.035 kPa at 30 litre/minute air (excluding the valve) is identical. Lack systems remain economical and are now fully satisfactory in clinical use. Replacement tubing (part number 8723–205) may be obtained from Medical and Industrial Equipment Ltd, Sowton Industrial Estate, Exeter EX2 7NA.

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Recovery times

Dr Cundy's comparison of recovery times after anaesthesia for termination of pregnancy. (*Anaesthesia* 1986; **41:** 93) was interesting. He compared the results of the use of intermittent thiopentone with propofol with which I have no experience. However, at Wistons Branch of the British Pregnancy Advisory Service over 100 000 terminations of pregnancy have been performed since 1971; intermittent methohexitone has been used in the great majority of cases with results similar to those described with propofol.

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The pulse oximeter and the collateral circulation

The oximeter can be used to check for adequate collateral circulation prior to an arterial line insertion. Allen's test[1] is the traditional test but, of course, is subjective and may not be reliable in some cases. A test can be conducted with the oximeter as follows. The finger sensor is placed on the patient and the radial and ulnar arteries are occluded in the usual way. The ulnar artery is then released, and the return of the pulse and saturation to normal, is checked. The oxygen saturation and the pulse wave should return to normal if the collateral circulation is adequate to maintain good oxygenation.[2]

A group of twenty patients (ASA 1) were first tested for collaterals by the modified Allen's test on both right and left hands and the results were noted. This test was repeated with pulse oximeter on both hands; all the testing was done by the author. The results of the two tests correlated extremely well. In 18 out of 20 cases, the prediction using the Allen's test was the same as that by the oximeter. In the two remaining cases, the Allen's test showed collaterals to be good, whereas the pulse oximeter indicated them to be poor.

Each test possesses certain advantages. The pulse oximeter can be utilised in comatose patients or in patients who, for one reason or another, cannot cooperate. It is also useful when arterial cannulation is required unexpectedly during an operation. Further, it does not necessitate adequate lighting for observation of blood return or free mobility of the wrist joint and hand. Finally, there is no need to depend on subjective observation. The Allen's test, on the other hand, is very convenient for pre-operative evaluation, since it does not require any special equipment. The study also demonstrates that it is perhaps a more reliable indicator than most anaesthetists assume.

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REGIONAL ANESTHESIA:

Techniques and Clinical Applications

HAROLD CARRON, GREGG A. KORBON, JOHN C ROWLINSON

1984, 208pp., $39.50/£33.00 (UK only)
ISBN: 0 8089 1654 8

This work is designed as a practical reference for all physicians and other professionals who use regional anaesthesia in their practice. Written by well-known teachers in the field, the text provides clearly defined guidelines on anatomical considerations, concise descriptions of surface landmarks and techniques for performing regional anaesthetic procedures.

The text is profusely illustrated including 16 colour illustrations; photographs of living subjects depict superficial anatomical landmarks and are accompanied by cut-away drawings illustrating the relationship of landmarks to nerves to be blocked.

ANESTHESIA AND THE GERIATRIC PATIENT

Edited by SUSAN WILSON KRECHEL

1984, 272pp., $42.50/£35.50 (UK only)
ISBN: 0 8089 1661 0

"This is an excellent book which is highly recommended not only as a useful compendium of information in a specific patient group but also as guide to anaesthetic problems which will be encountered with increasing frequency in the future."
— **The Lancet**

This book focuses on the anaesthetic management of elderly patients. It represents the state-of-the-art in this long neglected area by featuring a collection of the most pertinent and informative topics on the subject.

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This new pocket-sized guide provides a quick and thorough reference to the clinical uses of muscle relaxants.

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A PRACTICE OF ANESTHESIA FOR INFANTS AND CHILDREN

JOHN F RYAN, CHARLES J COTE, L DAVID TODRES, NISHAN GOUDSOUZIAN,

1985, 352pp., $67.50/£58.50 (UK only)
ISBN: 0 8089 1732 3

This book is a ready reference for the practical management of anaesthesia for paediatric patients. It provides more than the limited direction of a manual by emphasising the principles and psychology upon which the practice is supported.

Preoperative evaluation is approached with special emphasis on medical and psychological problems. Specialised areas, such as cardiac and neuroanaesthesia, have been treated separately, while subjects including malignant hyperthermia, regional anaesthesia and post-operative recovery care are approached in a practical manner.

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Volume 2: Cardiovascular Pharmacology

1983, 704pp., 243 illus., $78.50/£65.50 (UK only)
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Cardiac Anesthesia, Volume 2 is an indispensable "state-of-the-art" clinical, teaching and reference manual for practicing anaesthesiologists, anaesthesia residents, cardiac anaesthesia fellows, cardiologists, cardiac surgeons and all physicians and nurses dealing with cardiovascular problems. Because of the wide range of this book it is applicable to both cardiac and noncardiac patients.

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Anaesthesia, 1986, Volume 41, pages 785–788

Book reviews

Clinics in Anaesthesiology: Paediatric Anaesthesia 785
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Anaesthetic Management—A Rule-based Guide 785
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Edited by H. RAHN AND O. PRAKASH
Muscle Relaxants 788
Edited by R.L. KATZ

Clinics in Anaesthesiology: Paediatric Anaesthesia

Edited by E. SUMNER AND D.J. HATCH. Pp. 301, W.B. Saunders, 1985. £13.75.

Many new and useful texts devoted to paediatric anaesthesia have appeared in the last decade. Examples include an introduction, a manual, monographs, a textbook and a two-volume reference tome. Despite this luxury perfusion, the anaesthetist in paediatric practice could scarcely ask for a more interesting, readable and up-to-date review of the state of the art than this additional volume offers. The editors also intend it for the occasional paediatric anaesthetist, but it would take a true enthusiast to assimilate everything in this book.

Eighteen authorities from Britain, the United States of America, Australia, Canada and Sweden, have contributed 15 chapters covering a wide range of topics including clinical and practical management as well as pharmacological and physiological considerations.

Reading the work from cover to cover, your reviewer enjoyed not only the content but the readable style of each successive contribution until, that is, he reached that entitled Fluid Balance. Drs Bennett and Bowyer, with superb disregard for both style and syntax, have compressed the fruits of years of research and authorship into a formidable text which, whilst demanding and, I hope, repaying attention, seems (erroneously) twice the length of any other chapter.

Dr James' contribution on Emergencies is, by contrast, an outstanding combination of background material and practical recommendations. Indeed, most of the chapters can be read for pleasure as well as for information. Dr Zideman gives a refreshingly thorough and forward-looking review of paediatric resuscitation. Dr Feychting writes humanely of psychological aspects of paediatric anaesthesia and other contributions show how, increasingly, others recognise their importance. One chapter in particular is essentially a reference text, that by Dr Lynn, who brilliantly marshalls the vast array of congenital anomalies into a manageable, problem-orientated chapter with relevant advice for the anaesthetist and a number of photographic illustrations.

There are other illustrations: the graphs and line drawings are well reproduced, but the photographs of equipment are of poorer quality and do no service to an otherwise well produced and obviously carefully edited work. The index omits some topics covered in the text and thus is somewhat inadequate as a guide to what must be one of the best buys in the literature of this expanding field. The book would still be well worth reading at twice the price.

W.R. HAIN

Anaesthetic Management—A Rule-based Guide

By M.J. HARRISON, R.M. JONES AND B.J. POLLARD. Pp. 274, Butterworths, 1986. £13.50.

The authors' objective is to provide a pocket-sized book to guide the anaesthetist in the choice of suitable treatment and anaesthetic techniques for a patient scheduled for surgery with intercurrent medical disease and multiple drug therapy. The book is particularly aimed at the anaesthetist in training who does not have the experience and knowledge of his more senior colleagues. The authors have used the flow charts from a successful computer program which they developed at the University of Nottingham Medical School as the basis for this book. The first section of the book contains these flow charts and the reader is required to state the type of surgery to be undertaken, followed by details of the patient such as age and sex. The flow charts then lead the reader to a section on associated medical conditions. The reader is then referred to the relevant sections in the second part of the book, which discuss the problems and appropriate management of the patient.

The flow charts are easy to understand and use, and effectively guide the reader to the relevant information in the second part of the book. The quality of discussion and advice, although necessarily brief in a book of this size, is well presented and comprehensive. It is not controversial and represents standard anaesthetic practice. The scope of the book is wide; problems are discussed in reasonable depth and outline guidance is given on the choice of anaesthetic technique. It is difficult to find any common or indeed uncommon anaesthetic problem that has been left uncovered.

The rather unusual approach of this book, with its use of flow charts, is interesting; however, it is difficult to see a great advantage over a comprehensive index. What is suitable, and indeed necessary, for a computer program may not translate particularly well into book form. Nevertheless, the authors should be congratulated on the comprehensive nature of the advice given, which in almost every instance is valid and pertinent. There are, however, no references to further reading, although this could not be expected in a book of this nature. Apart from the use to which the authors intend the book to be put, it may also prove useful reading matter for anaesthetists preparing for their higher qualifications, in particular the Part I and III of the FFARCS diploma examinations.

JC. EDWARDS

Patient-controlled Analgesia

Edited by M. HARMER, M. ROSEN AND M.D. VICKERS. Pp. 199, Blackwell Scientific Publications, 1985. £18.00.

This book is described as the proceedings of the first international workshop on patient-controlled analgesia (PCA), held in the United Kingdom in June 1984. There were 25 participants from USA, the European continent and the UK; of these 14 were anaesthetists, nine were primarily associated with industry and two were physicists. There are four sections: on PCA as a research tool, on PCA and biofeedback systems (including a description of equipment), on PCA as a clinical regimen and on an assessment of the future of PCA. There is some reference to chronic pain and to obstetrics, but by far the greater part of the book is taken up with the problems of acute postoperative pain.

There is no doubt that postoperative analgesia, in the U.K. at least, is a mess. New drugs have been a profound disappointment; the best have provided, perhaps, some marginal advantage in some circumstances. None has provided what even the most sanguine could describe as a therapeutic revolution, most have been abandoned. Many anaesthetists have, not surprisingly, concentrated on essaying better methods of delivering what is currently available; of these, spinal administration of opiates and PCA stand out.

This book shows that PCA, though no panacea, is a method which gives some promise of advance, although it seems unlikely to provide anything approaching a radical and complete solution. There are formidable difficulties and some dangers. It is a criticism that the whole approach is overmechanistic. This criticism might be countered somewhat by saying that a state-of-the-art treatise about PCA is likely to be this way and that the contributors are entitled to assume a sound basic knowledge on the part of their readers. Despite this, it is a pity that the work of Beecher and the Harvard school hardly merits a mention. Again, the placebo effect, one of the most important features of analgesic therapy, receives less attention than it deserves. The subtlety of psychological reaction is not emphasised and the discerning reader must supply it for himself.

The book is basically a collection of papers on both theory and practice—the former being, perhaps, especially valuable. There is a good deal of repetition, but the book does provide a useful introduction to anyone considering using the method clinically or using it as a research tool. Indeed, at the moment the method itself is best considered experimental. There are a number of useful diagrams, the list of references is valuable and there is an adequate index.

J.E. UTTING

Atlas of Regional Anesthesia

By J. KATZ. Pp. 203, Prentice/Hall International 1985. £59.95.

This lavishly illustrated and expensive book is intended for the clinician without far-ranging experience of regional anaesthetic techniques; in the introduction it is suggested that successful neural blockade can be achieved by following the text and referring to the illustrations. This may be so, but anyone unwise enough to follow this suggestion without establishing a thorough working knowledge of indications for regional anaesthesia, pharmacology of local anaesthetic agents and adjuvant drugs, treatment of side effects and overdose, and all the principles of patient management before, during and after the procedure will undoubtedly end up in the gravest of trouble, since all these factors are largely ignored in the text. Such text as there is, is limited to a brief description of the basic anatomy for each block, with a cookbook explanation of how to perform it.

The lack of any substantial section on the basic principles of regional anaesthetic techniques disturbs your reviewer. For example, it is not enough in a text of this nature to gloss over the therapy of local anaesthetic overdose with the words 'the reader is referred to any standard text for details'. If the reader is expected to pay this amount of money for a textbook of local anaesthetic techniques, it seems reasonable to expect the coverage of the topic to be comprehensive, and the reader can hardly be blamed if he decides to invest in one of the standard texts referred to when this is not the case.

There can be no doubt that the author knows his subject and he gives advice that will be recognised to be reasonable by the experienced clinician, but which is ambiguous or insufficient for the tyro. The range of blocks illustrated is fairly comprehensive but eclectic in nature. There can be few, if any, indications for blockade of long buccal, masseter, phrenic, glossopharyngeal or vagus nerves in everyday practice. One wonders why the interscalene and infraclavicular approaches to the brachial plexus are described and not the technically easier and safer subclavian perivascular approach. Confusion will be compounded by the illustrations accompanying the descriptions of the axillary approach to the brachial plexus, and blockade of the musculocutaneous and intercostobrachial nerves, where the main nerves are either mislabelled or shown in incorrect positions both inside and outside the sheath.

One must question the wisdom of instructing the less experienced physician about blockade of the splanchnic nerves, the thoracic sympathetic chain and thoracic and cervical epidurals and spinals, especially as no illustration shows an intravenous infusion, and systemic hypotension is mentioned only with regard to cervical blocks. Set against this is the fact that many of these less common blocks are well illustrated and remind us of some useful and neglected blocks, but one is left wishing for more details.

Overall, this reviewer was disappointed. A great deal of time and effort has been expended on this book, which fails to cover the whole subject well enough to permit safe practice by the less experienced and which may be insufficiently comprehensive to appeal to the expert. There is a great deal of wasted space and the didactic style of writing omits many refinements and subtleties of technique that will lead to a higher success rate. There are no suggested references where this missing information may be obtained. It cannot be recommended in its present form and until a substantial expansion of the text is undertaken, other, older textbooks represent better value.

J.E. CHARLTON

Current European Anaesthesiology

Edited by R.M. JONES. Pp. 297, John Wiley & Sons 1985. £24.50.

Current European Anaesthesiology, or the Year Book of the European Academy of Anaesthesiology, is a collection of summaries of papers published in the European Literature followed by a reviewer's comments. The book is divided into five sections: pharmacology, medical problems, clinical practice, equipment and monitoring and resuscitation and intensive care. The journals chosen include the usual anaesthetic journals, together with some extremely obscure titles. The purpose of the book is apparently to increase the awareness of clinical research workers of work carried out in other European countries.

The pitfalls in producing a book of this type are many. The selection of suitable papers for review, the presentation of an adequate summary and the choice of a suitable reviewer are a few of the more obvious. Although 170 papers are reviewed, I found nothing of sufficient interest or importance outside the 'core' European journals to send me searching in Russian or Polish journals. Some of the summaries are inadequate and fail to give all the basic information, so that the validity of the reviewer's comments cannot be assessed. The list of reviewers at the beginning of the book contains several eminent anaesthetists, but readers should be aware that the majority assess very few papers; about half of the reviews are undertaken by staff of Guy's Hospital. There are a few reviewers from Guy's Hospital who assess papers from the same institution and, although they are never less than fair and objective, this is a totally unreasonable burden to place on any reviewer. Harsh criticism is rarely found, even when merited, so it was refreshing to find a German assessor who castigated a fellow countryman for having already published the same data in another journal! In those areas in which I have a particular interest some reviews were of a reasonable standard, but several missed major errors in the methodology of the studies and demonstrated a woefully inadequate background knowledge.

G.M. HALL

Acid-base Regulation and Body Temperature

Edited by H. RAHN AND O. PRAKASH. Pp. 165, Martinus Nijhoff. 1985. £34.75.

The stated aim of this book is to provide clinicians with the theories and strategies for the management of hypothermic patients. Most anaesthetists are familiar with the Rosenthal correction factors and the question to be asked is whether it is necessary to derive the actual $P\text{CO}_2$ at a hypothermic temperature, or to emphasise the CO_2 content to maintain a desirable H^+/OH^1 ratio. The latter is an easy aim as it is achieved by maintaining blood gas to achieve normal values when rewarmed to 30°C (the normal blood gas machine temperature).

The first four chapters deal with the physiology and biochemistry of acid-base; then three further chapters describe *in vivo* models and their therapeutic implications in cardiac surgery, infants and circulatory arrest.

Observations of core–shell temperature gradients lead the authors to believe that although pH and $P\text{CO}_2$ vary with hypothermia, the Donnan ratio and the hydroxy: hydrogen ion ratio remain unchanged. This is due to histidine imidazole which has a pK that is thermolabile (alphastat regulation). This apparently does not hold true for hibernating animals where pH and Pco_2 in most tissues are maintained at normal values, although the heart and liver follow alphastat regulation which maintains their enzyme function. Animals either adopt an alphastat strategy or a constant pH strategy, but the American ground squirrel can achieve both under different circumstances. Many meter pH by a receptor sensitive to alphamidazole. Details of carbon dioxide loading required to maintain constant pH in hibernators pass beyond relevant research into academic theories.

The conclusions are that alphastat regulation is the normal control mechanism in mammalian and reptilian tissue in response to temperature variation. Constant pH in hibernating animals is achieved by severe respiratory acidosis which may be used to inhibit various metabolic pathways. In human, induced hypothermia, catecholamine secretion is stimulated by acidosis and there are no separate mechanisms for the heart and liver. The advantages of the alphastat mechanism are the maintenance of pH gradients at the mitochondrion and in enzymatic function.

Swan applies this basic science to clinical hypothermic circulatory arrest, and gives four choices: pH stat, Pco_2 stat, alphastat and respiratory alkalosis. He argues that the literature justifies treatment with alkaline buffered perfusate and suggests that a pH of 7.7–8.1 is good for cardiac function at temperatures below 30°C, a conclusion which recent studies would certainly question. He also recommends a respiratory alkalosis.

The alphastat approach is equivalent to maintaining a constant Tco_2 and results in a constant pH and Pco_2 when corrected to 37°C. This is achieved by maintaining normothermic ventilation during hypothermia. The evolution of oxygen buffered perfusate solutions containing energy substrates is also described, although little attention is given to the dangers of glucose in ischaemic tissue.

The data in this book are important, but the clinical conclusions are a hard sell of an approach to acid-base balance pioneered by Swan and others. There is much repetition and heavy-handed criticism of conflicting studies. Nevertheless, *Acid-base Regulation and Body Temperature* is a major source of guidance for those who manage hypothermic patients.

R. Greenbaum

Muscle Relaxants

Edited by R.L. Katz. Pp. 305, Grune and Stratton Inc., 1985. £20.50.

When I read this book I had a feeling of *déjà vu*. The contents of the book have already been presented in 1984/85 *Seminars in Anesthesia*; many of the authors have also presented their material at various congresses and symposia and the majority of authors have also contributed to Norman's book on neuromuscular blockade, published 1985 in the *Clinics in Anaesthesiology* series. In fact, the illustrations used in the first chapter of this book and in Norman's book are identical.

The book is a collection of essays on various aspects of neuromuscular block. Most are good; however, like most multiple author books on a single topic, the chapters fail to progress to unveil an understandable concept of what happens when a neuromuscular blocking drug is given, how its action is terminated and how its effects may be altered by pathological events. The reader is given much information without interpretation; for example, is channel block a clinically significant event? What exactly is meant by desensitisation block (clearly Dr Choi sees it as the same as Phase II block; Dr Standaert does not, whilst Dr Lee says we should avoid using the term). How does the clinician know whether to use a 2-compartment model or a 3-compartment one when calculating the dose of relaxant, or should he perhaps ignore them all? In the clinical chapters, opinion is often presented as fact. Is it really sensible to advocate giving a potent histamine releasing drug to an asthmatic patient just because the author has not heard of any problems? Is the slow onset time following non-depolarising drugs really due to low muscle perfusion? Does suxamethonium really induce dysrhythmias in digitalised patients, or is it the preservative in the United States Pharmacopeial preparation? Should not anaphylactic reaction be mentioned as a complication of suxamethonium?

These criticisms are less a reflection upon the authors than on the nature of the book as a series of disparate essays on a common theme. It is the dilemma that all editors of multi-author books face. Unfortunately, today it is virtually impossible for any one person adequately to cover such a large subject, hence the dilemma.

Dr Katz has tried hard to get a sensible mix of authors; to do so he has trawled the same pool as Norman. Both books are similar in coverage; however, if I wished to have a reference book on neuromuscular block, I would prefer that of Professor Norman, since it is marginally more recent and contains many more non-American references. It seems that some American authors gave up reading European Journals around 1970!

S.A. Feldman

Anaesthesia, 1986, Volume 41, page 789

Index of computer programs

004.2.32

Authors B. Kumar and J.M. Watt (Department of Anaesthetics, Queen Elizabeth Hospital, Edgbaston, Birmingham 15).

Title MCQ.

Description This is a question file for use with the MCQ program published in Index of Computer Programs in 1983 by Watt and Dearlove.[1] The questions are designed to assess the knowledge of candidates appearing for Final FFARCS. The user is asked multiple choice questions requiring the answer 'True' or 'False', and is marked on his first attempt, although if he gives a wrong answer further tries are provided. After each question, explanatory notes are given and a score is presented at the end of the test.

This program can be played from cassette or disc.

Language BBC Basic.

Computing Facility BBC Model A or B (disk or tape).

Reference

1. WATTS JM, DEARLOVE OR. Birmingham General Hospital MCQ Program *Anaesthesia* 1983; **38**: 824.

004.3.31

Authors R.I. Francis and J.M. Watt (Department of Anaesthetics, Birmingham General Hospital).

Title ASTRUP.

Description ASTRUP is a teaching program to facilitate the understanding of the basic principles of acid-base balance. A normal set of blood gases is first presented, and the user is encouraged to change one parameter at a time and see the effect on the others. A graphical representation of the Astrup nomogram is also shown, and the effect of each change as to whether there is acidosis or alkalosis, and a respiratory or metabolic cause. The program has been accepted for use by the Faculty of Anaesthetists Scheme for Telesoftware Teaching and has been made generally available through the FASTT pages of Prestel.

Language BBC Basic.

Computing Facility BBC Model B computer.

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The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London, WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. An exact copy of the monthly section or various cumulative classifications of the Anaesthetic Literature published in the Journal can be obtained on application to him. References from January 1984 have been entered on data base and search facilities are also available. All communications about this matter should be addressed to Dr Kaufman please.

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Rapid adrenocorticotropic hormone test in practice. Retrospective review. MAY, M.E., CAREY, R.M. *American Journal of Medicine* 1985; **79:** 679.

Stimulus for vasopressin release during elective intra-abdominal operations. MELVILLE, R.J., FORSLING, M.L. *et al. British Journal of Surgery* 1985; **72:** 979.

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Natriuresis induced by arginine vasopressin infusion in sheep. Park, R.G., Congiu, M. *et al. American Journal of Physiology* 1985; **249** (Part 2): F799.

Factors of importance in the hyperglycaemia induced by upper abdominal surgery. Rutberg, H., Hakanson, E., Jorfeldt, L. *Clinical Physiology* 1985; **5:** 515.

Hyperinsulinaemia—a possible risk factor for cardiovascular disease in diabetes mellitus. Stout, R.W. *Hormone and Metabolic Research* 1985; **15:** 37 (Suppl).

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The effects of ACTH on the renin–aldosterone system in normotensive man. Whitworth, J., Butty, J. *et al. Clinical and Experimental Hypertension*. Part A Theory and Practice 1985; **7:** 1361.

The microcirculation of the renal medulla. Zimmerhackl, B., Robertson, C.R., Jamison, R.L. *Circulation Research* 1985; **57:** 657.

Treatment and medication

Frequency of diabetic ketoacidosis and hypoglycemic coma during treatment with continuous subcutaneous insulin. Audit of medical care. Bending, J.J., Pickup, J.C., Keen, H. *American Journal of Medicine* 1985; **79:** 685.

Deterioration in renal function in patients with chronic renal failure after treatment with captopril. Boner, G., Morduchowicz, Z. *et al. Israel Journal of Medical Sciences* 1985; **21:** 892.

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Complications of diabetes: prevalence, detection, current treatment, and prognosis. Clements, R.S., Bell, D.S.H. *American Journal of Medicine* 1985; **79:** 2.

How dangerous are diuretics? Freis, E.D., Papademetriou, V. *Drugs* 1985; **30:** 475.

Causes of death in diabetes mellitus. Fuller, J.H. *Hormone and Metabolic Research* 1985; **15:** 3 (Suppl).

Catecholamine, renin, aldosterone and arginine vasopressin responses to lower body negative pressure and tilt in normal humans. Effects of bromocriptine. Mohanty, P.K., Sowers, J.R. *et al. Journal of Cardiovascular Pharmacology* 1985; **7:** 1040.

Dystonia. Treatment with bromocriptine. Newman, R.P., Le Witt, P.A. *et al. Clinical Neuropharmacology* 1985; **8:** 328.

Effect of verapamil on renal plasma flow, glomerular filtration rate and plasma angiotension-II. Sorensen, S.S., Thomsen, O.O. *et al. European Journal of Clinical Pharmacology* 1985; **29:** 257.

Antihypertensive therapy in diabetic patients. Trost, B.N., Weidmann, P., Berettapiccoli, C. *Hypertension* 1985; **7** (Part 2): 102 (Suppl).

Effects of packed cell volume reduction on renal haemodynamics and the renin–angiotensin–aldosterone system. Wallis, P.J.W., Cunningham, J. *et al. Clinical Science* 1986; **70:** 81.

Pharmacokinetics of the loop diuretic piretanide in renal failure. Walter, U., Rockel, A. *et al. European Journal of Clinical Pharmacology* 1985; **29:** 331.

Pain

Physiology

The use of electromyography to quantify muscle pain. Mylinski, N.R., Buxbaum, J.D., Parente, F.J. *Methods and Findings in Experimental and Clinical Pharmacology* 1985; **7:** 551.

Treatment and medication

Epidural ketamine for control of postoperative pain. Islas, J.-A., Astorga, J., Laredo, M. *Anesthesia and Analgesia* 1985; **64:** 1161.

Postextraction pain relief in children: a clinical trial of liquid analgesics. Moore, P.A., Acs, G., Hargreaves, J.A. *International Journal of Clinical Pharmacology, Therapy and Toxicology* 1985; **23:** 573.

Newer methods of delivery of opiates for relief of pain. Slattery, P.J., Boas, R.A. *Drugs* 1985; **30:** 539.

Development of the y-aminobutyric acid neurotransmitter system in the rat cerebral cortex during repeated administration of ethanolamine O-sulphate. Sykes, C.C., Horton, R.W. *Journal of Neurochemistry* 1985; **46:** 213.

Other

Treatment and medication

Inhibition of shivering in man by thermal stimulation of the facial area. Mekjavic, I.B., Eiken, O. *Acta Physiologica Scandinavica* 1985; **125:** 633.

Anaesthesia, 1986, Volume 41, pages 796–804

News and notices

Stop Press. *Readers of this section are also referred to the Stop Press page at the end of this section.*

Obituaries

Fisher, David Keir, FFARCS, formerly anaesthetist at Glasgow Dental Hospital and Royal Infirmary. Qualified in dentistry and medicine from the University of Glasgow in 1923.

Fraser, Rosemary Anne, MB, BS, FFARCS, DA, consultant anaesthetist to the High Wycombe District Health Authority. Qualified from the Middlesex Hospital in 1951.

Holland, Charles Bennett, DSC, MD, ChB, FFARCS, consultant anaesthetist to the Ipswich Hospitals from 1950 to 1976. Qualified at the University of Manchester in 1936.

Knott, James Andrew, MB, ChB, formerly consultant anaesthetist at Warneford Hospital, Leamington Spa. Qualified at University of Birmingham in 1922.

Association of Anaesthetists of Great Britain and Ireland

The Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA, England. Telephone: 01–631 1650 (Ansafone service available out of office hours).

Standing notices

Full details of the activities of the Association are published in the January edition of *Anaesthesia* (106–111). These include details of membership publications of the Association, educational and historical information.

Future meetings of the Association

Annual Scientific Meetings

1986—London, 18–19 September.
1987—Sheffield, 10–11 September.
1988—Southampton, 15–16 September.

Linkman Conferences

1986—London, 17 September.
1987—Sheffield, 9 September.
1988—Southampton, 14 September.

Research grants

Research grants may be made towards a salary for a doctor or technician, or the cost of equipment. Candidates should write for full information to the Honorary Secretary and applications should be made on the special form designed for this purpose. Grants are unlikely to exceed £5000 per annum to an individual or department. Applications may be submitted any time during the year for consideration at the next meeting of the Research and Education Committee. This Committee meets three times each year.

Association travel grants

Association travel agents are available towards the cost of a tour, either at home or abroad, including teaching research or study, but neither for the purposes of attending meetings of societies nor for taking up posts abroad. Grants of up to £500 may be awarded.

Applications should be made on a special form which may be obtained from the Honorary Secretary and may be submitted at any time during the year, provided sufficient time is allowed for their consideration by the Research and Education Committee.

Undergraduate prize of the Association

The Prizes are offered for the most meritorious essays written by an undergraduate medical student at a university in Great Britain or Ireland. The competition is in two classes with prizes in each class of £100, £50 and £25.

Class 1—aspects of basic science of anaesthesia.
Class 2—clinical aspects of anaesthesia.

Rules

Essays should be submitted before 1 April 1987. The number of entrants from any one medical school is limited to a maximum of five. The Association recognises that most medical schools already offer prizes to medical students for an essay on a topic related to the specialty and has therefore decided that the winning of a local prize will not preclude the writer from entering for the Association prize.

Essays should be prepared according to the general format of the 'Notice to Contributors' at the end of each issue of *Anaesthesia*. Three copies of the essay should be forwarded to the Honorary Secretary.

Regional and Specialist Society Meeting Dates

The Honorary Secretary once again appeals to the secretaries of regional and specialist anaesthetic societies to try to check that their proposed meetings do not conflict with other previously arranged events to their mutual detriment. Dr A. Padfield, Royal Hallamshire Hospital, Sheffield S10 2RX, sub-editor of the National and local events section, has advance notice of meeting dates beyond those published in that section.

Competence to practise

The Association of Anaesthetists of Great Britain and Ireland and the Royal College of Psychiatrists are cooperating in a scheme to help sick anaesthetists early in their illness.

The system depends upon voluntary reporting by colleagues and is not coercive. It must be emphasised that this scheme is supplementary to existing controls. Fitness to practice may be impaired through illness and the sick doctor for various reasons may not take any steps to remedy the situation. The scheme provides machinery whereby confidential psychiatric help can be offered to the ailing doctor from a source outside his own Region.

The reporting clinician should contact the office of the Association of Anaesthetists to ascertain the name of a referee (Dr P.J. Helliwell, Dr D.C. Howat, Dr S.A. Mason) and need not identify himself to the office staff. The reporting clinician will be given the name, telephone number and availability of the referee. Preferably, a second clinician will also be required to confirm the report to the referee. The referee will then contact a psychiatrist from another Region nominated by the College of Psychiatrists from a prepared list: the psychiatrist will then get in touch with the potential patient.

No further information will be transmitted through the system unless the potential patient does not accept the offer of a visit to the nominated psychiatrist. In that case, the reporting physician(s) will be informed after a month that treatment has not been accepted.

Suitable arrangements have been made for confidential treatment of the doctor–patient in another Region and for the reimbursement of travel expenses.

Anaesthesia in the third world countries

The Association of Anaesthetists, through its International Relations Committee, receives many requests to provide lectures and clinical instructors for Departments of Anaesthesia throughout the developing world.

There is considerable variety in the requirements of different locations, but the general policy of the Association is to provide an educational rather than a purely service commitment. Vacancies currently exist in Nigeria, Ghana, Zimbabwe and Zambia and are mostly of one year's duration (although occasionally shorter periods are required).

Anyone interested in service in a developing country who has the FFARCS diploma should write to Chairman of the International Relations Committee, Dr R.J. Eltringham, Department of Anaesthesia, Gloucestershire Royal Hospital, Gloucester GL1 3NN.

Recent publications of the Association of Anaesthetists of Great Britain and Ireland

Fees for anaesthetists in private practice. January 1986.
Post-anaesthetic recovery facilities. 1985.
Professional references in the National Health Service. Guidance and proforma, 1985.

These, and earlier publications, are available from the Association office.

The Junior Anaesthetists' Group of the Association of Anaesthetists of Great Britain and Ireland

All junior members of the Association are members of the Group. The Group committee has representation on various committees of the Association and Faculty.

Committee

Chairman: Dr G.W. Hamlin (*1 Grange Park Close, Leeds, LS8 3BU. Tel. (0532) 659114.* Council of the Association. JCHTA Manpower and Working Party of Faculty, Advisory Panel and Faculty Tutors).

Honorary Secretary: Dr Laurie Allan (*Pentland Grove House, Seafield by Roslin, Midlothian, Edinburgh EH25 9RQ. Tel. (031) 445 2313.* Council, Hospital Junior Staff Committee, Council of Royal Society of Medicine, Editorial Board.).

Committee members: Dr A.D.J. Nicholl (*2 Hardwick Close, Ipswich IP4 5XB. Tel. (0473) 718432.* Faculty Education Committee, Safety Committee, Linkman Coordinator), Dr I. Woods (*40 Coppice Avenue, Sale, Cheshire, M33 4WB. Tel. (061) 962 8860.* International

Relations Committee). Dr Nancy Redfern (*Westfield House, Acomb, Hexham, Northumberland. Tel. (0434) 607444.* Specialist Societies Committee). Dr Deborah Schiller (*4 Lisa Court, Downsland Road, Basingstoke, Hants. Tel. (0256) 477885.* CCHMS, Association Working Party on Manpower). Dr Anne Blyth (*7 Cleveden Gardens, Glasgow G12 0PU. Tel. (041) 34 9974*). Dr G. Fitzpatrick (*46 Melborn Road, Bishopstown, Cork, Eire. Tel. (010) 353 21 4654*), Dr S. Linter (*Southampton*), Dr D. Paul, (*Edinburgh*). Dr K.C. Lowry (*10 Sandhill Park, Co. Armagh, BT66 7AX Tel. (07622) 22628.* Coopted for Northern Ireland Meeting).

Representative of Council: Dr R.J. Eltringham (*Gloucester*).

The Annual Scientific Meeting

The 1986 Meeting was held at Cardiff from 8–10 April and was attended by 230 Juniors. The meeting was preceded by the second annual meeting of the Junior Linkmen which was attended by 37 linkmen. The Scientific programme was as follows. First session, *Clinical trials*; Chairman: Dr P.W. Thompson, Professor M.D. Vickers, Planning the work; Professor M. Rosen. Getting it done; Professor W.W. Mapleson. Analysing the results; Dr J.N. Lunn. Writing it up. Second session, 'The Registrars' Prize Papers'; Chairman: Dr T.B. Boulton. Five papers were presented. The winning paper was that by Drs A. Allison (and B.E. Smith) *Sciatic nerve blockade using a low power peripheral stimulator*; Dr R.S. Laishley, (A.C. O'Callaghan and J. Lerman), was second with *Effect of dose and concentration of rectal methohexitone for the induction of anaesthesia in children.* Third session, *Presentation*; Chairman: Dr T.R. Austin. Professor W.W. Mapleson, Preparing scientific material; Professor R. Marshall, The use of audiovisual aids; Mr A. Levy, Public speaking techniques. Fourth session: *Patient controlled analgesia*; Chairman: Dr J.N. Horton, Professor M. Rosen, Philosophy and development; Dr G.A.D. Rees, Use in Obstetrics; Dr M. Harmer, Postoperative use; Dr J.M. McCarthy, Future developments.

The Annual General Meeting of the Junior Group was attended by 116 members.

The *Pinkerton lecture* was given by Professor Emeritus K. Rawnsley whose subject was 'The sick doctor'. Fifth session, *Medicolegal hazards of surgery and anaesthesia*; Chairman: Professor Emeritus W.W. Mushin C.B.E., Professor B.H. Knight, Some forensic facts; Dr W.D. Wylie. Some practical do's and don'ts: Dr P.W. Thompson, Training to avoid trouble. Sixth session; *Practical procedures 1.*; Chairman: Dr J.N. Lunn, Professor M. Cousins, Complications of regional anaesthesia: Dr T.R. Austin, Regional anaesthesia in trauma patients.

Seventh session, *Practical procedures 2*; Chairman: Dr J.S. Davies. Dr K.R. Murrin and Dr R.S. Vaughan, Difficult tracheal intubation; Dr W.S. Ng and Dr I.P. Latto, Central venous cannulation.

The delegates were invited to attend the *6th Mushin Lecture* which took place during the meeting. This was given by Professor M. Cousins (*Flinders University, Australia*) and was entitled, What does the specialty of anaesthesia offer in the management of acute and chronic pain?

Future meeting

1987—Belfast, 8–10 April (Junior Linkman Meeting, April 7).
1988—Nottingham, 5–8 April.

Faculty of Anaesthetists of the Royal College of Surgeons of England

The Faculty of Anaesthetists of the Royal College of Surgeons of England, 35–43 Lincoln's Inn Fields, London WC2A 3PN. Telephone: 01–405 3474

Faculty News

Election of Dean and Vice Dean

At a meeting of the Board of Faculty held on 18th March, 1986 Dr Aileen K. Adams was re-elected Dean and Dr P.W. Thompson was elected Vice Dean for the year from June, 1986.

Election to the Council of the Royal College of Surgeons, England

At a meeting of the Board of Faculty held on 18th March, 1986 Dr Aileen K. Adams, Dr P.W. Thompson, and Professor D. Campbell were elected as representatives of the Faculty on the Council of the Royal College of Surgeons, England for the year from July, 1986.

Election to the Board

As a result of the election held on 5th March, 1986 Professor M. Rosen, Professor D. Campbell and Dr J.S.M. Zorab have been re-elected and Dr D.J. Hatch, Professor C.J. Hull, and Dr S.M. Willatts have been elected to the Board of Faculty. 1497 Fellows returned valid voting papers and in addition there were 13 invalid voting papers.

Election to the Fellowship

The following were elected to the Fellowship at a meeting of the Board held on 18th March, 1986. Dr B. Barry (*Sydney*, Australia); Dr H.H. Bendixen (*New York*, USA); Professor W. Dick (*Mainz*, West Germany); Professor P.A. Foster (*Stellenbosch*, South Africa); Dr A. Kilpatrick (*Lancaster*); Dr C. Parsloe (*Sao Paulo*, Brazil); Dr H. Ruben (*Copenhagen*, Denmark); Dr W.K. Slack (*Harlow*).

Faculty Adviser

Dr J.A. Bushman, the Bernard Johnson Adviser in Postgraduate Studies, would like to remind all anaesthetists in training that he is available for advice in careers and study. An interview can be arranged by application to the Faculty office (tel: 01–405 3474 ext. 45).

Examination news

The following have been elected as *new examiners* for the FFARCS examination for the academic year 1986–87. *Part I:* Dr T.H.L. Bryson, Dr J.E. Charlton, Dr A.A. Gilbertson, Dr J.E. Goodwin, Dr J.L. Jenkinson, Dr I. McLellan, Dr A. Padfield and Dr J. Thorburn. *Part II:* Dr J.A.W. Wildsmith. *Part III:* Professor J.W. Dundee.

Examination results

At the Part III FFARCS held in January 1986, 61, of the 356 candidates, were successful. At the Part I FFARCS held in March 1986, 151 of the 309 candidates were successful.

Faculty of Anaesthetists of the Royal College of Surgeons in Ireland

The Faculty of Anaesthetists of the Royal College of Surgeons in Ireland, 123 St Stephen's Green, Dublin 2.
Telephone: Dublin 780200 (Ext 268).

Dean: Dr P.W. Keane.
Vice-Dean: Dr D.C. Moriarty.
Honorary Secretary: Dr D.F. Hogan.
Honorary Treasurer: Dr J.C. Cooper.

Faculty Lectures, 1986

Autumn, September 26. Speakers: Drs W.P. Blunnie (*Dublin*), P. Cream (*Belfast*), J.D. McAdoo (*Cork*), C. O'Hagan (*Dublin*).
Winter, December 12. Dr L.J. Saidman (*California*).

FFARCSI Examinations, 1986

Part 1, October 17 (closing date, September 5); part 2, October 24 (closing date, September 12); part 3, November 28 (closing date, October 17). *Revision course* (Part 2) October 8–15.

For further information please write to the Honorary Secretary, Faculty of Anaesthetists, Royal College of Surgeons in Ireland, Dublin 2.

Section of Anaesthetics of the Royal Society of Medicine

Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE. Telephone: 01–580 2070

President: Dr Aileen K. Adams.
Secretaries: Dr I.M. Verner (*Department of Anaesthetics, The Middlesex Hospital, Mortimer Street, London W1N 8AA*), Dr G.M.C. Patterson (*Oxford*).

Meetings of the Section are held on the first Friday in the month and are held at 1 Wimpole Street, London W1M 8AE, at 5.30 p.m.

Fellows of the RSM are welcome to bring guests if they wish.

Specialist Societies

British Association for Immediate Care (BASIC)

Chairman: K.C. Easton, OBE.

Secretary: Hamish McLeod (*The Hope, Moffat Dumfriesshire. Tel: Moffat 20314*).

Society of Anaesthetists of the British Forces in Germany

President: Professor J.P. Payne (London).
Secretary: Major S.T. Inglis, FFARCS, RAMC (BMH Rinteln, BFPO 20 Germany).

Association of Cardiothoracic Anaesthetists

Honorary Secretary: Dr R.D. Latimer (*Papworth Hospital, Papworth Everard, Cambridge CB3 3RE. Tel: 0480 830541*).

Future meetings

1986—12 December, London.
Information: Dr R. Feneck (*London Chest Hospital, Bonner Road, London E2 9JX*).
1987—Spring Meeting—Cambridge.
Information: Dr I. Hardy (*Papworth Hospital, Papworth Everard, Cambridge CB3 8RE*).
Autumn Meeting—Liverpool.
Information: Dr J.C. Richardson (*Broadgreen Hospital, Thomas Drive, Liverpool L14 3IB*).

Association of Dental Anaesthetists

President: Dr T.M. Young (*Manchester*).
Secretary: Dr M.A. Skivington (*Department of Anaesthetics, Poole General Hospital, Poole, Dorset BH15 2JB*).
Assistant Secretary/Editor: Dr M.E. Ward (*Oxford*).

Future Meetings

1987—17 January, Queen Elizabeth Hospital, Postgraduate Medical Centre, Birmingham.
Information: Dr P.J. Tomlin.
11 July. Plymouth.
Information: Dr F.S. Keddie.

Intensive Care Society

Chairman: Dr Sheila M. Willatts (*Bristol*).
Meetings Secretary: Dr C.J. Hinds (*St Bartholomew's Hospital*).
Secretary/Treasurer: Dr D. Ryan (*Intensive Therapy Unit, Freeman Hospital, Newcastle upon Tyne NE7 7BE*).

Future meetings

1986—1 November, Hospital for Sick Children, London.
1987—9–11 April. Exeter University.

The Intractable Pain Society of Great Britain and Ireland

Chairman: Dr H. Rafferty (*Dublin*).
Vice-Chairman/Chairman Elect: Dr K. Budd (*Bradford*).
Honorary Secretary: Dr T.P. Nash (*Basingstoke District Hospital, Aldermaston Road, Basingstoke, Hampshire RG24 9NA*).

Prize Essay

An annual competition is held for the best essays related to pain relief. Submissions to the Honorary Secretary by 31 August 1986. Essay contests are judged in two groups. Doctors in training; and Society members.

Future meetings

1986—20 September—Joint Meeting of the British Medical Acupuncture Society, Royal Society of Medicine.
1987—Annual General Meeting and Scientific Meeting, Liverpool.
Hosts: Drs C. Wells and S. Lipton.

Neuroanaesthetists' Travelling Club

Information: Dr S.B. Foulds, Salford Health Authority, Peel House, Albert Street, Eccles, Manchester M30 0NJ.

Obstetric Anaesthetists' Association

President: Dr D.D. Moir (*Glasgow*).
Honorary Secretary: Dr J. Thorburn (*Department of Anaesthesia, The Queen Mother's Hospital, Yorkhill, Glasgow G3 85H*).
Treasurer: Dr A.P. Rubin (*London*).
Minute Secretary: Dr B.R. Wilkey (*Cambridge*).
All UK membership enquires to Dr J. Thorburn, please.

Future meetings

1986—4–5 September, Coleraine, N. Ireland.
Host: Dr J. Moore.

Information about meetings is available from the host.

Association of Paediatric Anaesthetists

President: Dr G.W. Black (*Belfast*).
Honorary Secretary: Dr P. Morris (*Royal Manchester Children's Hospital, Pendlebury, Manchester M27 1HA*).

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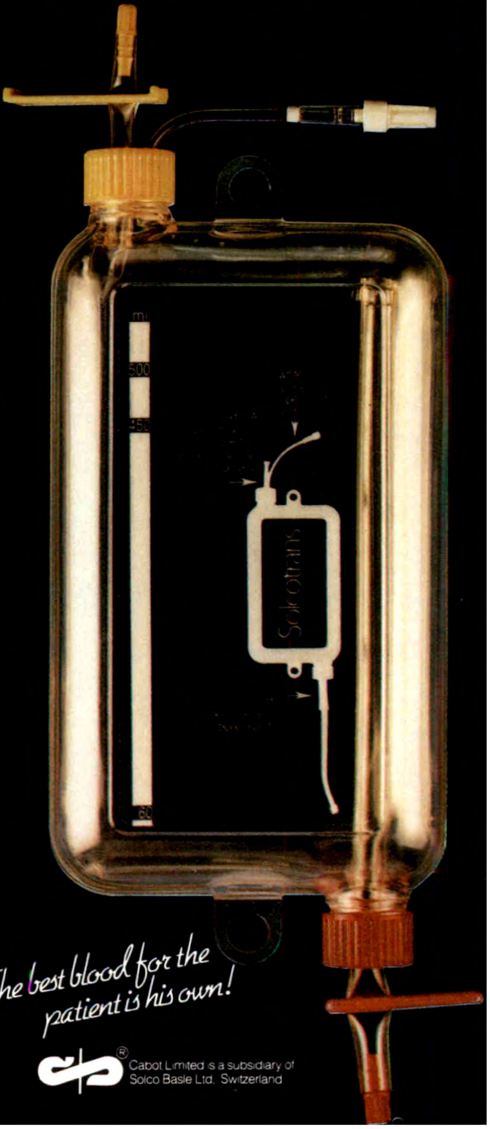

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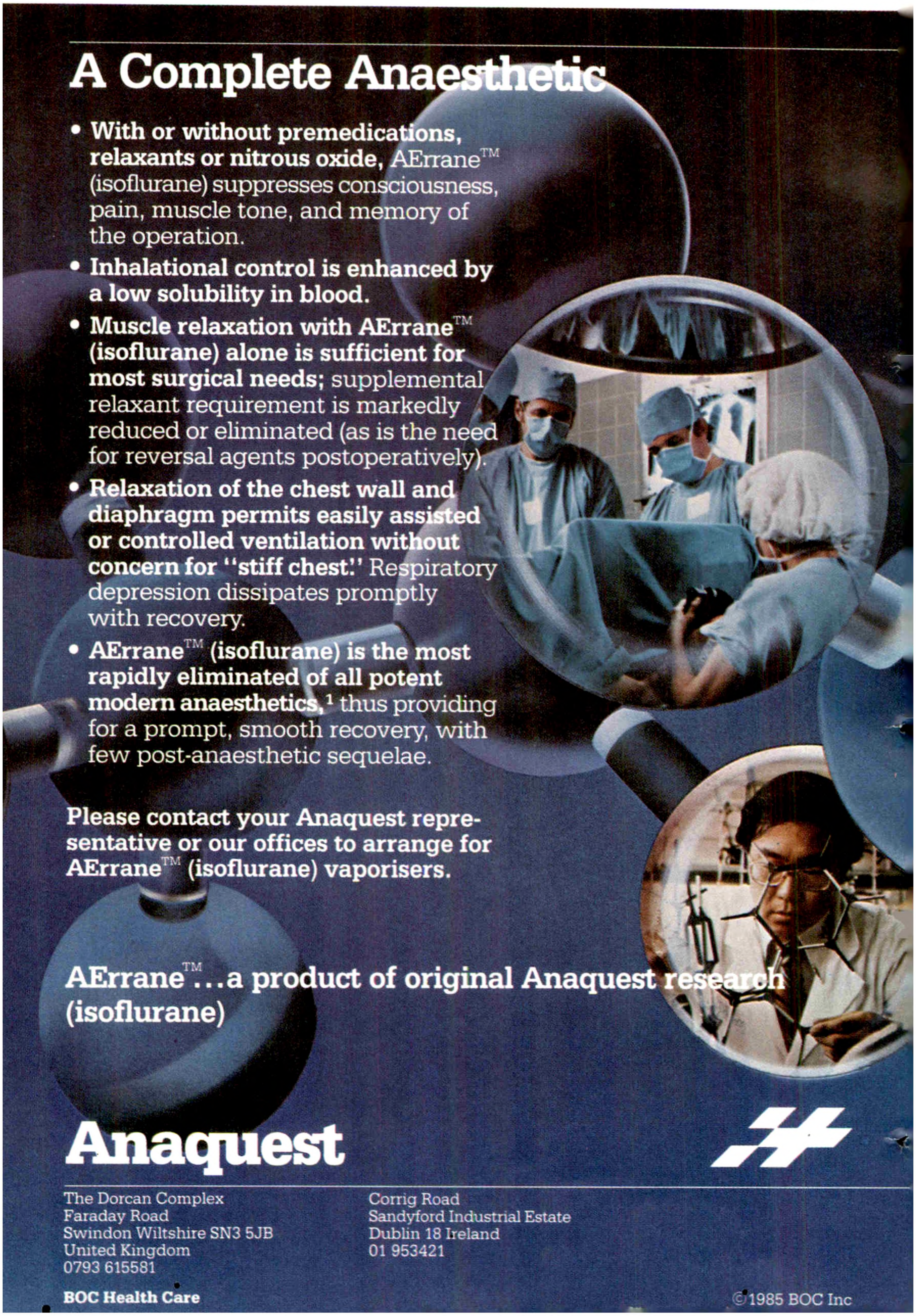

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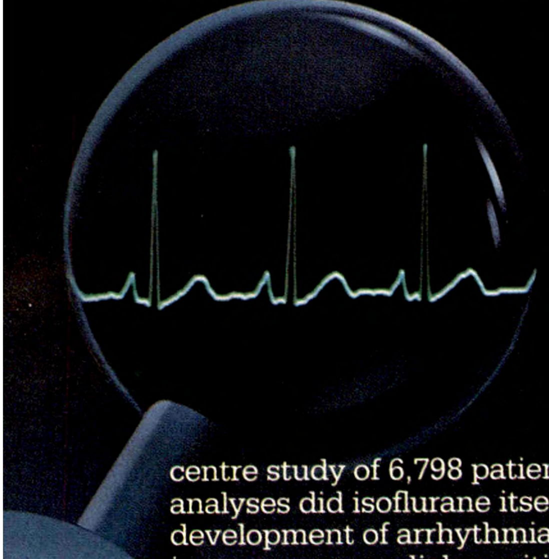

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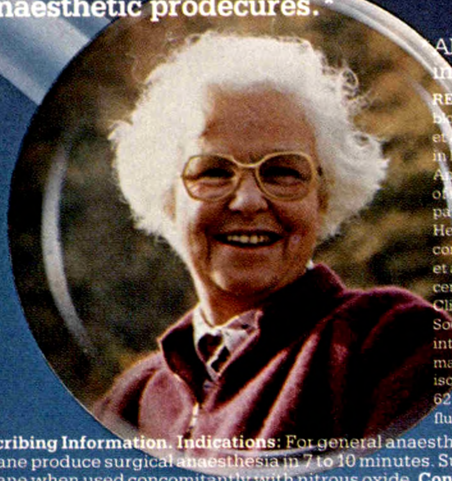

*AErrane™ (isoflurane) is not approved for use in obstetrics.

REFERENCES: 1. Cromwell TH, et al: Forane uptake, excretion and blood solubility in man. Anesthesiology 35:401-408, 1971. 2. Stevens WC, et al: The cardiovascular effects of a new inhalation anesthetic, Forane, in human volunteers at constant arterial carbon dioxide tension. Anesthesiology 35:8-16, 1971. 3. Linde HW, et al: Cardiovascular effects of isoflurane and halothane during controlled ventilation in older patients. Anesth Analg 54:701-704, 1975. 4. Mallow JE, et al: Hemodynamic effects of isoflurane and halothane in patients with coronary artery disease. Anesth Analg 55:135-138, 1976. 5. Lam AM, et al: Cardiovascular effects of isoflurane-induced hypotension for cerebral aneurysm surgery. Anesth Analg 62:742-748, 1983. 6. Levy W: Clinical evaluation of isoflurane: Cardiac arrhythmias. Can Anaesth Soc J 29 (suppl): 828-834, 1982. 7. Johnston RR, et al: A comparative interaction of epinephrine with enflurane, isoflurane and halothane in man. Anesth Analg 55:709-712, 1976. 8. Suzukawa M, et al: Use of isoflurane during resection of pheochromocytoma. Anesth Analg 62:100-103, 1983. 9. Adams RW, et al: Isoflurane and cerebrospinal fluid pressure in neurosurgical patients. Anesthesiology 54:97-99, 1981.

Prescribing Information. Indications: For general anaesthesia. **Dose:** Inspired concentrations of 1.5 to 3.0% AErrane produce surgical anaesthesia in 7 to 10 minutes. Surgical anaesthesia can be maintained with 1.0 to 2.5% AErrane when used concomitantly with nitrous oxide. **Contraindications:** Known sensitivity to AErrane or other halogenated anaesthetics; known or suspected genetic susceptibility to malignant hyperthermia. **Side Effects:** Hypotension, respiratory depression, arrhythmias, elevated white blood count, shivering, nausea, vomiting and ileus have been reported. **Product Licence Number:** 5247/0002.

Association of Anaesthetists of Great Britain and Ireland

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The Annual Meeting

This was held at the Hallam Tower Post House Hotel, Sheffield, on 21 and 22 March 1986.

The Scientific programme was as follows:

Session 1. Chairman: Dr G.W. Black (*Belfast*). *Contributions from the Children's Hospital, Sheffield.* Mood prediction during induction of anaesthesia in children undergoing day case surgery. Gell, I.R. and Harris, R.W. A comparison of temazepam elixir and trimeprazine syrup for the premedication of children. Harris, R.W. and Gell, I.R. Tracheomalacia in association with tracheo-oesophageal fistula: management and anaesthetic implications. Conroy, P.T. and Bennett, N.R. Congenital trachea stenosis: case report and review. Gerrish, D.P.

Session 2. Chairman: Dr N.R. Bennett (*Sheffield*). Anaesthetic management of severe croup. Lopez, T.J. (*Cape Town*). Acute epiglottis in children. Ekstrom-Jodal, B. and Strand, V. (*Gothenberg*). Therapeutic approach in very severe airway stenoses. Mantel, K. and Butenandt, I. (*Munich*). Anaesthesia in children with osteogenesis imperfecta—experiences with 43 consecutive cases. Fosel, Th., Berg-Seiter, S., Woersdorfer, O., Vetter, U. and Altemyer, K.-H. (*Ulm*).

Session 3. Chairman: Dr P. Morris (*Manchester*). Sacral epidural anaesthesia. Busoni, P. (*Florence*). Loss of resistance or nerve stimulator for anterior approach to sciatic nerve block? McNicol, L.R. (*Glasgow*). Rectal meptazinol for postoperative analgesia. Govaerts, M.J.M. (*Brussels*).

Session 4. Chairman: Dr A. Murray Wilson (*Sheffield*). A study into the effects of maternal presence at induction of general anaesthesia in children. Hickmott, K.C., Shaw, E.A., Goodyer, I. and Baker, R. (*Manchester*). Which infants really need premedication? Buttner, W., Breitkopf, L. and Czorny-Rutten, M. (*Herne*). The use of analgesia in the under one year age group. Results of a questionnaire. Dorman, F.M., Sumner, E. and Purcell-Jones, G. (*London*). Dreaming and perioperative complaints in paediatric surgical patients. Hobbs, A.J. (*Liverpool*).

Session 5. Chairman: Dr G.H. Bush (*Liverpool*). Spontaneous breathing, respiratory drive and timing at different end-tidal halothane concentrations in children. Lindahl, S.G.E., Yates, A.P. and Hatch, D.J. (*London*). Pulmonary ventilation and gas exchange before and after correction of congenital cardiac malformations. Yates, A.P., Lindahl, S.G.E. and Hatch, D.J. (*London*). The Ruben circle system in paediatric anaesthesia. Nightingale, D.A. and Hobbs, A.J. (*Liverpool*). Capnography in small children. Hutton, P., Hughes, D.G. and Stokes, M.A. (*Bristol*). Effects of rectal thiopentone and methohexital on carbon dioxide tension in infant anaesthesia with spontaneous ventilation, Larsson, L.E., Nilsson, K., Andreasson, Se and Ekstrom-Jodal, B. (*Gothenberg*).

Future meetings

1987—6–7 March. Annual Meeting, Leeds.
12–13 June. Third APA Seminar, London. This meeting is open to all anaesthetists interested in paediatric anaesthesia.

Information from the Honorary Secretary.

Plastic Surgery and Burns Anaesthetists

President: Dr C.C.M. Howie (*Bangour*).
Honorary Secretary: Dr F.J.M. Walters (*Department of Anaesthetics, Frenchay Hospital, Bristol BS16 1LE*).

Enquiries about membership to the Honorary Secretary, please.

Future meeting

1986—27 September, Whiston, Merseyside.
Information: Dr C.S. Ince (*Department of Anaesthetics, St Helen's Hospital, St Helen's, Merseyside WA9 3EA*).

The Russell Davies and Stuart Laird Prize

The Society wishes to announce that this prize, £200, has been generously donated by Abbott Ltd. The prize will be awarded for an essay connected with anaesthesia and plastic and burns surgery and is open to any career anaesthetist in the National Health Service. Applications are invited for the prize which is to be awarded in October 1986. Further details are obtainable from the Honorary Secretary.

Anaesthetic Research Society

Chairman: Professor A.A. Spence.
Honorary Secretary: Dr A.R. Aitkenhead (*University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW*).

Future meetings (closing dates for papers)

1986—4–5 July (May 23). University of Newcastle.
15 November (3 October). St Bartholomew's Hospital, London.
1987—20 March (6 February). University of Oxford.

Special notice

Abstracts are photoreduced and must be submitted on a preprinted form, which is available from the Hon. Secretary. All correspondence and abstracts should be sent to the Hon. Secretary.

Resuscitation Council (UK)

Chairman: Mr A. Marsden.

Secretary: Dr D.A. Zideman (*Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS*).

Advanced life support

Posters which illustrate the Council's recommendations for Advanced Life support are now available.

Home news and notices

Honours

Dr P. Morris (*Manchester*) has been appointed to an Honorary Visiting Professorship in the Department of Aeronautical and Mechanical Engineering, University of Salford.

Election

Professor D. Campbell (*Glasgow*) has been elected as Vice-President of the Royal College of Surgeons of England.

Academic appointment

Dr J.G. Jones, FRCP, FFARCS, (*Northwick Park*) has been appointed to the chair of Anaesthetics in the University of Leeds.

Professor J.W. Downing, FFA(SA) (*Durban*, South Africa) has been appointed to the foundation chair of Anaesthetics in the University of Nottingham.

Consultant Appointments

Dr C.P. Beeky—Wessex RHA.
Dr H. Daya—West Midlands RHA.
Dr R.J. Summerfield—Wessex RHA.

National and local events

July 1986

4–5 *Anaesthetic Research Society at Newcastle.* *Information:* Dr A.R. Aitkenhead, University Department of Anaesthesia, Leicester Royal Infirmary, Leicester, LE1 5WW.

14 *FFARCS Part 1/DA(UK).* Vivas begin.

August 1986

12 *FFARCS Part 2.* Applications due.

27–29 *Edinburgh Anaesthesia Festival.* *Information:* Department of Anaesthetics, Royal Infirmary, Edinburgh EH3 9YW.

September 1986

5 *FFARCS (Ireland) Part 1.* Applications due.

8–12 *Faculty Introductory Course in Clinical Anaesthesia.* *Information:* Mr S.N. Alan, Secretary, Faculty of Anaesthetists, Royal College of Surgeons, 35/43 Lincolns Inn Fields, London WC2A 3PN.

12 *FFARCS (Ireland) Part 2.* Applications due.

17–19 *Association of Anaesthetists Linkman, AGM and Annual Scientific Meeting, London.* *Information:* Honorary Secretary, 9, Bedford Square, London, WC1B 3RA.

23 *FFARCS Part 2.* Papers.

26 *FFARCS (Ireland).* Faculty Lecture. *Information:* Honorary Secretary, Faculty of Anaesthetists, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin 2.

26 *Intractable Pain Society*, jointly with British Medical Acupuncture Society. *Information:* Dr T.P. Nash, Basingstoke General Hospital, Hampshire RG24 9NA.

27 *Plastic Surgery and Burns Anaesthetists*, at Whiston, Merseyside. *Information:* Dr C.S. Ince, St Helen's Hospital, St Helens WA9 3EA.

27 *Southern Society of Anaesthetists*, at Epsom. *Information:* Dr R.P.H. Dunnill, Poole General Hospital, Dorset BH15 2JB.

29–17 Oct *Faculty Course on Anaesthetics.* *Information:* Mr S.N. Alan, Secretary, Faculty of Anaesthetists, Royal College of Surgeons, 35/43 Lincoln's Inn Fields, London WC2A 3PN.

October 1986

3 *FFARCS Part 1/DA(UK).* Applications due.

3 *Clinical Trials in Anaesthesia*, Kelvin Conference Centre, Glasgow.

Information: Secretary, University Department of Anaesthesia, Glasgow Royal Infirmary, 8–16 Alexandra Parade, Glasgow G31 2ER.

8–15 *FFARCS (Ireland) Revision Course. Part 2.* *Information:* Honorary Secretary, Faculty of Anaesthetists, Royal College of Surgeons in Ireland, St Stephen's Green, Dublin 2.

17 *FFARCS (Ireland) Part 1 begins.*

17 *FFARCS (Ireland) Part 3.* Applications due.

18 *Postgraduate Study Day*, jointly organised by the Faculty and the Association.

20 *FFARCS Part 2.* Vivas begin.

22 *Whole-day Symposium*, Respiratory Problems in Anaesthesia, Walsgrave Hospital, Coventry. *Information:* Dr C.J. Knickenberg, Department of Anaesthetics, Walsgrave Hospital, Coventry, CV2 2DX.

24 *FFARCS (Ireland) Part 2 begins.*

International congress calendar

1986

15 August. Msida, Malta. *IV Annual Conference of the Association of Anaesthesiologists.*

Information: Secretary, PO Box 15, Msida, Malta.

20–23 August. Hamilton, New Zealand. *1986 Conference of Anaesthetists of New Zealand.*

Information: The Organising Committee, CANZ 86, Department of Anaesthesia, Waikato Hospital, Hamilton, New Zealand.

27–30 August. Rotterdam, The Netherlands. *First European Congress of Paediatric Anaesthesia.*

Information: Dr H.J. Manschot, Department of Anesthesiology, Sophia Children's Hospital, Gordelweg 160, 3038 GE Rotterdam, The Netherlands.

2–5 September. München, West Germany. *Association of Cardiothoracic Anaesthetists. Anaesthesia for Cardiac Patients.*

Information: ISACP/INTERPLAN, Sophienstrasse, 8000 München 2, West Germany.

3–6 September. Malmo, Sweden. *Fifth Congress of the European Congress of Regional Anaesthesia.*

Information: Anestesikliniken, Malmo Allmanna Sjukhus, S 21401 Malmo, Sweden.

3–6 September. Rotterdam, The Netherlands. *Fourth International Symposium on Computing in Anaesthesia and Intensive Care.*

Information: Omar Prakash, MD, Thorax Centrum, PO Box 1738, 3000 DR Rotterdam, The Netherlands.

3–6 September. Paris. *Joint Meeting of The European Society of Pneumology and the European Society for Clinical Respiratory Physiopathology.*

Information: Convergences SEP-SEPCR, 16 Rue Jean-Jacques Rousseau, 75001 Paris, France.

4–5 September. Southampton, England. *International Conference/Workshop on 'Blood vessel imaging using ultrasound techniques'.*

Information: Mr K.N. Humphries, Medical Physics Department, Level D, Centre Block, Southampton General Hospital, Southampton, S09 4XY.

16–19 September. Haifa, Israel. *14th International Congress of the Israel Society of Anesthesiologists.*

Information: Congress Secretary, PO Box 50006, Tel Aviv 61500, Israel.

20–25 September. Hong Kong. *7th Asian and Australasian Congress of Anaesthesiologists.*

Information: 7th AACA Secretariat, International Conference Consultants, 1st Floor, 57 Wyndham Street, Central, Hong Kong.

24–26 September. Leicester. *Royal College of Surgeons Annual Provincial Meeting (Anaesthetic Section).*

Information: Royal College of Surgeons of England, 35–43 Lincoln's Inn Fields, London, WC2A 3PN.

29–30 September. Beijing, China. *Symposium on Anaesthesiology.*

Information: 7th AACA Secretariat, International Conference Consultants, 1st Floor, 57 Wyndham Street, Central, Hong Kong.

18 October. London. *Postgraduate Study Day (Joint Meeting with the Faculty.*

Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

18–21 October. Perth, Western Australia. *Annual Meeting of the Australasian Society of Anaesthetists.*

Information: Secretariat ASA, PO Box 345. Paddington, NSW 2021, Australia.

20–22 November. Cleveland, Ohio. *Anesthesia and the Heart Patient.*

Information: Lisa Politi, Center for Continuing Medical Education, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, Ohio 44106, USA.

23–28 November. Florianopolis, Santa Catarina. *33rd Brazilian Congress of Anesthesiology.*

Information: Carlos A. Da Silva Junior, MD, Alameda Adolfo Konder 25, 88.000 Florianopolis, Santa Catarina, Brazil.

27–30 November. Grenoble, France. *4th International Conference on Disaster Medicine.*

Information: Ste Intern, Medecine de Catastrope, PO Box 59, CH 1213, Petit Lancy 2 France.

1987

7–9 May. Paris. *VI Annual Meeting of the European Society of Regional Anaesthesia.*

Information: M.A.P.A.R., Département d'Anesthesiologie, Hopital de Bicetre, 94270 Kremlin-Bicetre, France.

16–22 May. Perth, Australia. *Faculty of Anaesthetists and the Royal Australasian College of Surgeons Annual General Scientific Meeting.*

Information: Administrative Assistant, Faculty of Anaesthetists, R.A.C.S., Spring Street, Melbourne, 3000 VIC.

20–25 June. Montreal, Canada. *XIII International Symposium on Cerebral Blood Flow and Metabolism.*

Information: Sorelcomm (1985) Inc., Conference Secretariat, 1425 Dorchester Boulevard West, Montreal, Canada, H3G 1T2.

20–23 July. London. *2nd International Symposium of the History of Anaesthesia.*

Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.

23–25 July. Oxford, England. *50th anniversary of the founding of the Nuffield Department of Anaesthetics.*

Information: Nuffield Department of Anaesthetics, Department GP/87, Radcliffe Infirmary, Oxford OX2 6HE.

2–7 August. Hamburg, West Germany. *Vth World Congress on Pain.*

Information: Vth World Congress on Pain, c/o Hamburg Messe und Congress GmbH Congress Organization, Postfach 30 24 80, 2000 Hamburg 36, West Germany.

23–28 August. Sydney, Australia. *10th International Congress of Pharmacology.*

Information: The Secretariat, 10th IUPHAR Congress, GPO BOX 2609, Sydney, NSW 2001, Australia.

1988

1–6 May. Brisbane, Australia. *Faculty of Anaesthetists and the Royal Australasian College of Surgeons Annual General Scientific Meeting.*

Information: Administrative Officer, Faculty of Anaesthetists, R.A.C.S., Spring Street, Melbourne, 3000 VIC.

22 June–28 May. Washington, DC. *9th World Congress of Anaesthesiology.*

Information: American Society of Anesthesiologists, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

15–16 September. Southampton, England. *Annual Scientific Meeting of the Association of Anaesthetists of Great Britain and Ireland.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9, Bedford Square, London WC1B 3RA.

Anaesthesia, 1986, Volume 41, page 805

Safety information bulletin

Cape Waine Mark II ventilator—Gardner Oxygen failure device (SIB(86)28)

This device (ref. 2300) developed faults which allowed nitrous oxide to flow through the oxygen flowmeter when the oxygen supply was disconnected. This is the reverse of what should happen with this device. All Cape Waine Mark II ventilators which are on a service contract with Penlon Limited should have been fitted with a new device (ref. 5530). If ventilators are not on such a service contract they may still have a potentially hazardous oxygen failure device fitted. The new device holds a perspex cover with three screws, in the old device the perspex top is itself threaded. If there is any doubt please contact Penlon Limited.

Metal tracheal tube introducers (SIB(86)26)

One copper stilette fractured and a small piece of the stilette was left in the trachea. It is suggested that all malleable metal stilettes should be closely examined before and after use to identify cracking or work hardening.

Ferrari's Wright Respirometer (SIB(86)24)

A damaged respirometer resulted in a small component becoming detached; this bypass jet could have reached the patient's airway. In the event of damage it is suggested that recalibration should be considered at shorter intervals than those currently recommended by the manufacturer.

Errata

Anaesthesia, 1986, Volume 41, pages 294–295

The stability of preservative-free morphine in plastic syringes

R. J. BRAY, P. A. DAVIES AND J.A. SEVIOUR

The second sentence of the summary should read as follows:

The morphine concentration remained at 100% (within 1.5%) of the control values over 36 hours and demonstrates that the concentration of morphine is not reduced with time in these circumstances.

Anaesthesia, 1986, Volume 41, page 227

Book review

A Calculus of Suffering by M.S. PERNICK
In the review of this book by Dr J.E. Riding the final paragraph should read as follows:

This study of how profoundly the discovery of anaesthetics affected the profession and its patients in nineteenth century America inspires the thought that a comparably broad study of nineteenth century Britain would be valuable in itself and might well unearth a very different story.

THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

Ordinary Membership (*United Kingdom and Ireland only*)

Voting membership of the Association (the only effective body representing anaesthetists' interests in non-academic matters).

The right of attendance at the Annual General and Scientific Meetings and all other meetings of the Association of Anaesthetists.

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Voting membership of the Association.

Representation of the Council of the Association. The Chairman and Secretary of the Junior Group sit on Council as voting members.

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Retired Members: who receive *Anaesthesia* **£10** (there is no subscription for those who do not).

How to apply for membership

Fill in the application form on the other side of this page.

Have it countersigned by two members of the Association, one of whom must be an Ordinary Member.

Tear out the page and send it to the address indicated overleaf.

Do not send money with your application

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

APPLICATION FOR MEMBERSHIP

to

The Association of Anaesthetists of Great Britain and Ireland
9 Bedford Square,
London WC1B 3RA, England

(This application will be considered by Council at its next meeting. NO MONEY should be sent in the meantime. After acceptance of the application by Council, the Hon. Secretary will notify the applicant of Council's decision and the amount of subscription payable in the current financial year.)

........................19

To the Honorary Secretary,
Association of Anaesthetists of Great Britain and Ireland

I (full name).. offer my name as a candidate
BLOCK LETTERS

for (a) MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) JUNIOR MEMBERSHIP of the Association (*please delete categories not applicable*)*

I hold the following appointment(s) as an anaesthetist (*please state grade if in the National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia*):

....

....

....

Qualifications (with dates)..

....

(Signed)...

Address..

....Hospital Tel. No:.................................. ....

....Home Tel. No:..

We, being Members† of the Association, nominate as a candidate for MEMBERSHIP/OVERSEAS/ASSOCIATE/JUNIOR MEMBERSHIP

....

1. (Signed)...
(NAME IN BLOCK LETTERS)
Address..
BLOCK LETTERS

2. (Signed)...
(NAME IN BLOCK LETTERS)
Address..
BLOCK LETTERS

* See the reverse of this page for details of membership categories.

† One sponsor must be an Ordinary Member of the Assocation.

Notice to contributors to *Anaesthesia*

Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Articles accepted become copyright of *Anaesthesia.*

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

Dr J. N. Lunn, Editor of ***Anaesthesia****, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (U.K.).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author.

The manuscript should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page.

THE TITLE PAGE

The name of the author and the address to which proofs and other correspondence is to be addressed should appear in the top left-hand corner of the sheet.

The main title should be restricted to five words if this is possible. It should be typed in capitals across the centre of the title page.

A subsidiary title of not more than 12 words may be supplied if this is considered to be necessary. This should be typed in lower case immediately beneath the main title.

The names of the authors should be typed IN CAPITALS across the title page immediately beneath the titles without degrees or designations. Initials should precede the surname. One forename may be given in full according to the author's preference. If there is more than one author the word 'AND' should be placed before the name of the last author.

A line should be typed across the title page below the author(s) name(s) in capitals.

The author(s) name(s) degrees and designations should be typed in lower case below the line. Initials and/or forename should precede the name of each author and his degrees, without full stops between letters, and appointment (e.g. Consultant, Registrar, etc.) should follow it.

A full postal institutional address should follow the names, degrees and appointments. Correspondence will normally be addressed to the first author but, if it is desired to direct correspondence other than to the first author, or if different authors belong to different institutions or departments, a separate sentence should be added: this should start on a new line and begin 'Correspondence should be addressed to ...' and a full postal address should follow.

SUMMARY AND KEY WORDS

Start a new sheet

The second page should carry a summary of not more than 150 words. The summary should state the purpose of the study or investigation, basic procedures, main findings and their statistical significance, and the principal conclusions.

Do not use abbreviations except for units of measurement (e.g. mg, cm, etc.).

Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus.* The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

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(*continued overleaf*)

THE TEXT

Start a new sheet

The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction, Methods, Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia.*

Headings: three steps of heading may be used in typescripts:

(i) CAPITALS across the centre of the page.

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These should be typed at the left hand side of the page above the paragraph which they precede.

(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the first sentence of the paragraph.

ACKNOWLEDGMENTS

Start a new sheet

Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

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Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble space typing.

Use the form of reference adopted by the U.S. National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscript submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

The references must be verified by the author(s) against the original documents.

Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOYEN CE, *comps. Textbook of virology; for students and practitioners of medicine and other health sciences.* 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L, SWARTZ MN Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: WB Saunders, 1974: 457–72.

Agency publication

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Newspaper article

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Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

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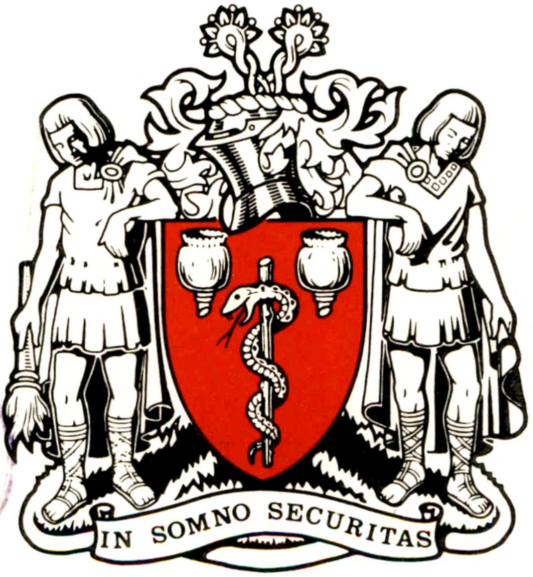

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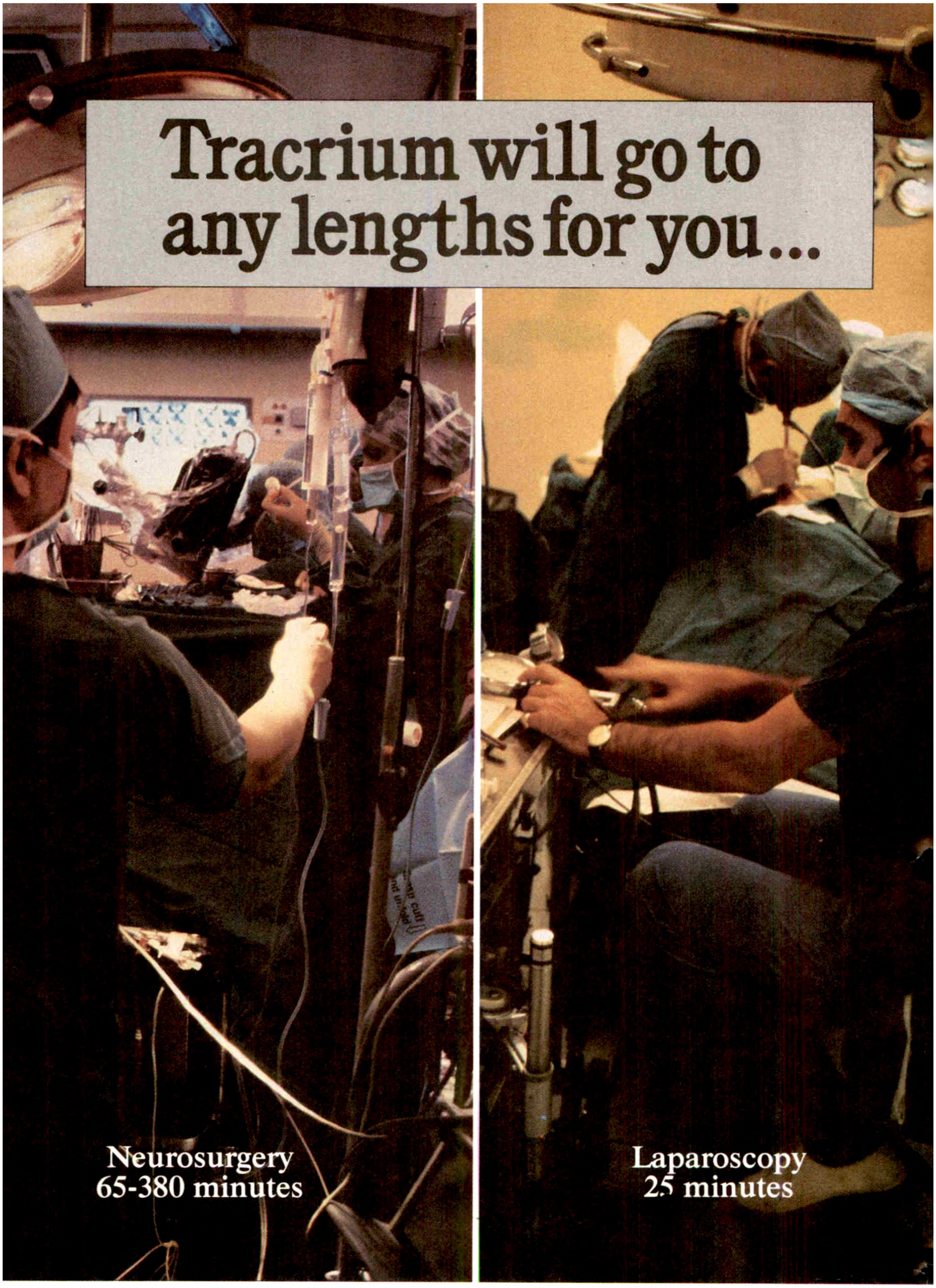

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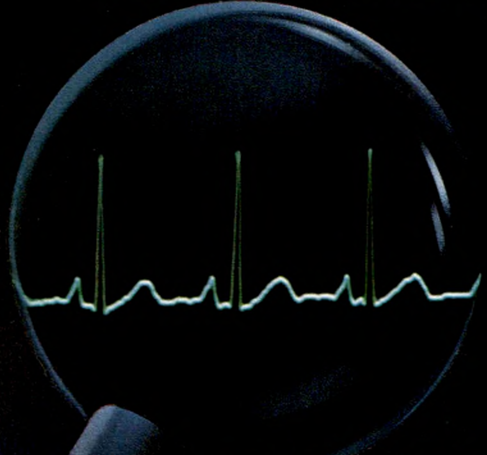

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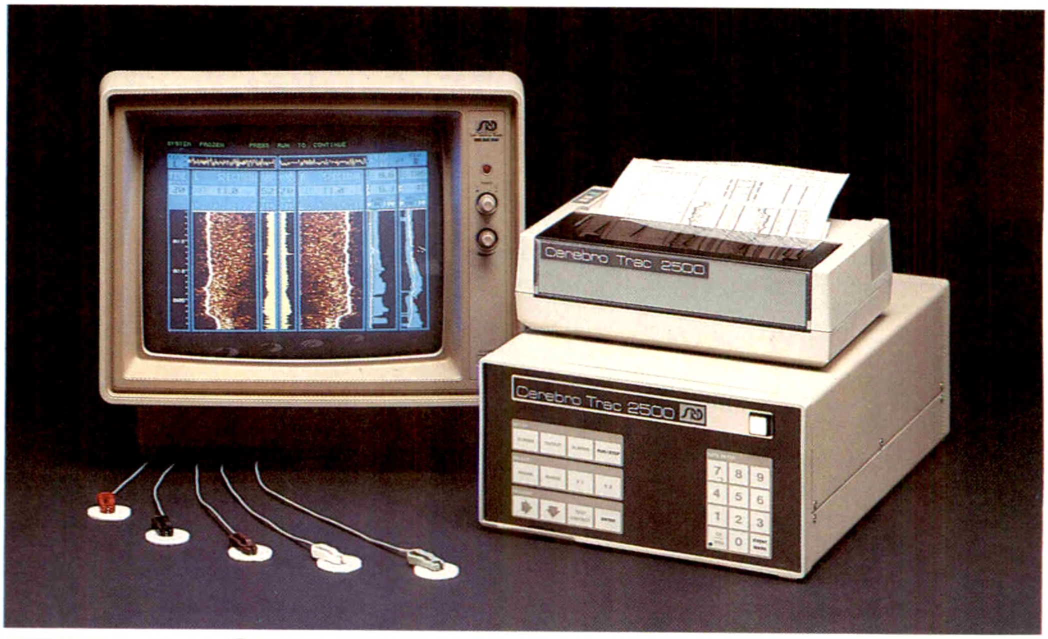

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Editorial

Alarms and excursions

The failure of doctors and nurses to observe a change in a patient's condition is a common feature of many medical accidents. In the attempt to improve safety, systems were developed which measure variables in the patient or in machines attached to them, but the attendant's attention was then divided between patient and variable display. The next step was to add warning devices to the measurement systems to produce what we know as monitors. So many monitors are being employed, however, that problems with the multiplicity of alarm signals generated by their warning devices are becoming increasingly common.[1-3]

It must be appreciated that a warning device set properly to indicate that a patient *may* be at risk will necessarily be activated on many occasions when the actual danger is slight.[3] On each occasion when the variable being measured crosses the alarm limit, the patient either will or will not be damaged. We would be irresponsible if we were to set the alarm limit at a level at which the probability of damage was high, so that in clinical practice, it is set where the probability of damage is low. Two inevitable consequences follow this decision; firstly, at this level, the probability that damage will *not* occur is high (false alarms will be common), and secondly, that since this level will be close to the normal, or safe, range for the measurement, the frequency with which the limit will be crossed will be higher than if it were set further from the normal range. When one sets the alarm limits on a monitor, therefore, one is implicitly balancing an assessment of the probability that the patient will be damaged if the limit is crossed against factors such as distraction from more important tasks (looking at the patient or other measurements), irritation, and legal attitude (aggressive/defensive!). Anything which tips the balance in favour of the setting of alarm limits at levels where the risk of damage is low is potentially beneficial to the patient, but the long term answer to the most effective use of warning devices will require several approaches.

On the physiological side, a better appreciation of the relative importance of different alarms requires that the chain of consequences between the event that activates each warning device and that which produces damage in the patient must be analysed. In assessing priority, particularly if intelligent, or 'smart', alarm systems are being devised, temporal factors must be considered and, in particular, the time taken by the attendant to correct the alarm condition. Paradoxically, warning devices on variables measured on the patient (e.g. heart rate or oxygen saturation) indicate that a physiological derangement already exists and that the time before damage occurs may be short, whereas the time required to correct the problem may be relatively long because the number of possible causes is large. In contrast, measurements made on machines attached to the patient (e.g. loss of oxygen pressure) predict that a physiological derangement and damage may ensue while their correction time is short because the cause is clearcut.

On the engineering side, warning devices could feed their signals to a common outlet which would indicate both the existence and nature of the problem. This approach is being pursued actively in the United States of America, where several companies are producing anaesthetic machines which incorporate central alarm systems which accept alarm signals from devices measuring ventilator variables, gas pressures and composition from the machine, plus signals from other patient monitors. This approach may be less practical in the ICU, where equipment is less standardised and more mobile and where movement around the bed is already hampered by 'the spaghetti syndrome'.[5]

On the psychological side, the alarm signals themselves should be improved. The difficulty about visual signals is that they must be observed to be effective and the attendants' reliability in this matter is already discredited. Many warning devices produce sounds, therefore, but these are usually loud, continuous or intermittent high pitched noises which sound continuously as long as the alarm condition persists, so that the commonest initial response to current alarm noises is to silence them, and only

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then to tackle the problem that has activated the alarm. Another common response is to disable the alarm altogether.[6]

A British Standards Committee (HCC 16, Medical alarms and signals) has enlisted the help of the Medical Research Council's Applied Psychology Unit at Cambridge to devise a set of audible warning signals which alert staff without startling and which impair communication and concentration less. These new signals are characteristic multi-note 'calls' which last for a second or two and are repeated at intervals of about 10–15 seconds. Each note is composed of several harmonics to reduce the likelihood of masking and to make them easier to locate. The pause after the call has sounded is to allow staff to deal with the problem without interruption.

Seven calls have been produced, each of which has two forms; a faster, urgent form to indicate emergency situations which demand immediate action and a slower, less aggressive form for situations which require prompt attention. The total number of pairs has been limited to seven because it has been shown that the ability to recall the significance of different sounds diminishes above this number.[7] It has been proposed that one pair be allocated for general use on central alarm systems and one each for devices which make measurements relating to oxygenation, ventilation, circulation, temperature, drug infusion and artificial perfusion (e.g. dialysis or heart lung machines). These proposals fit well with the findings of a recent Canadian survey[8] and it is hoped to start clinical trials with the new sounds in the near future.

If this system were adopted for monitors throughout the hospital, staff would only have to learn the warning sounds once and would then be able to recognise instantly the type of problem whenever an alarm was heard. This contrasts with the present situation, when any manufacturer may put whatever sound he chooses on any variable, with the result that staff have to learn the significance of a new set of sounds whenever they move, or (a rare event!) whenever a new item of equipment arrives.

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Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 12 September 1986 for January 1987, 12 December 1986 for April 1987 and 13 March 1987 for July 1987.

Supplementary News and Notices sections will be published in the other issues but they will contain only material which requires publication before the next full News and Notices section.

Anaesthesia, 1986, Volume 41, pages 809–815

The work of the Leeds Malignant Hyperpyrexia Unit, 1971–84

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Summary

A detailed account of the procedure of muscle biopsy for screening patients suspected of being susceptible to malignant hyperpyrexia is given, together with a review of the results obtained from 1127 patients screened over the last 14 years. The information should help anaesthetists to discuss the investigation fully with probands and other members of their families before referral for further specific investigation.

Key words

Hyperthermia; malignant.
Muscle, skeletal.

On 7 February 1971 the University Department of Anaesthesia was asked advice about anaesthesia for a young man who required a hernia repair. In 1960 his sister had received anaesthesia for correction of subluxation of the patella and had died of an episode later suspected to be malignant hyperpyrexia (MH). A laboratory investigation of tissue taken from his rectus femoris muscle revealed a halothane-induced contracture at 37C.[1] Further family studies confirmed that the halothane contracture was a consistent feature of MH-susceptible (MHS) muscle and could be used as a diagnostic test.[2] Kalow and colleagues[3] had previously demonstrated an increased propensity by MHS skeletal muscle to develop contracture on exposure to caffeine at room temperature. The halothane and the caffeine contracture tests have complemented each other and, over the intervening years, have been used to establish the role of *in vitro* muscle studies in the screening of susceptibility to MH.

There has been a continuous expansion of the investigation unit since its inception in 1971 and it now provides a national screening service. This paper provides a detailed description of the clinical and laboratory aspects involved in the muscle biopsy procedure and also reviews the 1127 patients screened up to the end of 1984. Ording, Ranklev and Fletcher[4] have published an inventory of the work of the Danish and Swedish MH investigation units.

Referral and selection of patients

Referral of probands (the first member of a family to have a suspected MH reaction) and their relatives has increased since 1971 as both MH and the Leeds unit have become better known. The clinical aspects of the referred case or family are diverse, ranging from an unexplained postoperative death of a distant relative many years ago to a textbook example of a fulminant

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MH episode. Thus it may be difficult, with the available clinical details, to give an informed opinion as to whether MH had occurred or not without recourse to muscle biopsy and *in vitro* screening.

In view of the implications of a provisional diagnosis of MH, not only for the proband but also for all other family members, it is important that the diagnosis of MH in the proband is confirmed or refuted. All surviving probands are investigated, unless they are younger than 10 years of age or too ill, in which case confirmation of their MH status can only be obtained indirectly by testing their parents, one of whom must have transmitted the abnormal genotype. If the first parent is shown to be MHS the second parent is assumed to be normal as MH is a dominantly inherited rare condition (see later). When the first investigated parent is negative the spouse is biopsied.

Likewise, deceased probands are genotyped indirectly. Assuming a dominant inheritance, the chances of other family members being affected can be predicted using Mendelian principles. Members having a 50% probability include children, parents and siblings of any known MHS subject; as far as possible, investigations are restricted to the 50 percentile probability group. This may seem a rather costly and laborious procedure, but the alternative of labelling the whole family MHS is most unsatisfactory as a typical four generation family may contain 628 members. On average, only 8% of the family need be biopsied to identify the 3.8% who will be affected.[5]

Clinical management

Patients accepted for muscle biopsy stay for two nights in hospital. Routine pre-operative investigations include electrocardiograph, chest X ray, haemoglobin and electrolytes. On occasions other investigations may be required, such as an electromyogram and muscle enzymes, to exclude abnormalities which can be associated with other muscle diseases. Rectal temperature is recorded 2-hourly overnight prior to the biopsy operation, to provide a baseline, and then hourly post-operatively until the evening. No premedication is given, to avoid pharmacological contamination of the muscle, and a pre-operative serum creatine phosphokinase (CK) sample is taken immediately prior to induction of anaesthesia.

Muscle biopsy procedure

The muscle biopsy is taken from the motor point of the left vastus internus muscle, identified by nerve stimulation both percutaneously (pre-operatively) and directly using a sterile electrode. The advantages of using the motor point are as follows: the identification of a consistent site, providing between-patient comparability; the presence of the neuromuscular junction is presumed to be important if muscle relaxants are used in the tissue bath; its presence ensures adequate twitches on electrical stimulation in the tissue bath, because muscle tissue is most effectively stimulated via the neuromuscular synapse; muscle histology incorporates an assessment of fibre diameter size and variation. At the motor end plate region the fibre diameter variability is less than towards the ends of the muscle where fibres progressively narrow into their tendinous insertions.

The operation, which lasts 20–30 minutes, is performed under general anaesthesia. Our preferred anaesthetic technique includes intermittent thiopentone and fentanyl, with 50% nitrous oxide and oxygen from an uncontaminated machine using a Magill attachment. If a clean machine is unavailable, Entonox is used with a Water's semi-open system. Occasionally, epidural anaesthesia with plain bupivacaine is employed if general anaesthesia is thought to be contraindicated. More recently a 'three-in-one' block of the femoral canal[6] has been used. Rectal temperature, ECG, blood pressure, heart rate and respiratory rate are monitored and recorded.

Complications of this technique are rare, but do include laryngospasm if anaesthesia is inadequate and muscle rigidity associated with excessive fentanyl, although the total dose of fentanyl (around 0.05–0.2 mg per adult) is less than that previously described as causing rigidity by Hill and colleagues.[7] Both these difficulties can be aborted by tracheal intubation using atracurium, but this destroys the end plate specificity to electrical stimulation. The advantages of general anaesthesia are ease and reliability; most patients prefer to be asleep, despite possible MH susceptibility; children are often emotionally unsuited to local anaesthetic techniques; if a nerve block is inadequate, a local infiltration technique with local anaesthetic can attenuate the *in vitro* response by local diffusion onto the surface of the muscle; postoperatively, patients are reassured to

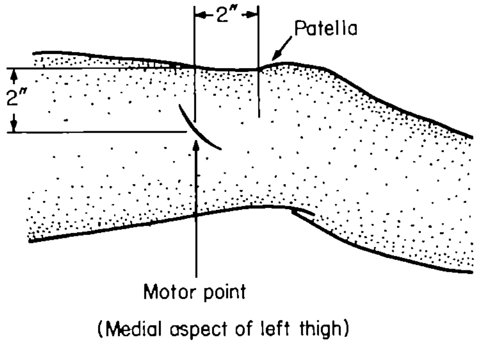

Fig. 1. Langer's skin incision over the left vastus internus muscle.

find that safe anaesthesia is available to them if required in the future.

Muscle specimens are taken through a 2-inch incision which follows Langer's lines circumferentially around the knee, overlying the vastus internus muscle (Fig. 1). Exposure of the muscle is improved by placing a sandbag under the knee.

Management of biopsied muscle tissue

At least three muscle samples are taken for *in vitro* screening and stored in Kreb's solution at room temperature in the laboratory. The Kreb's solution is aerated with carbogen (95% oxygen, 5% carbon dioxide). Other specimens are taken for histological studies. One sample is taken for biochemical studies and is therefore immediately frozen in liquid nitrogen. The wound is closed in layers using 2/0 chromic catgut for deep fascia, 2/0 plain catgut for superficial fascia and a continuous prolene subcuticular beaded skin stitch.

In vitro testing

A clean fasicle is dissected from the muscle sample under a dissecting microscope using a × 6 objective and is then placed in the tissue bath (Fig. 2). One end is attached, with the use of 5/0 mersilk to a 100 gm Devices strain gauge, (no. 4151, Ormed Engineering Ltd). The tissue bath, maintained at 37C, is continuously perfused with Kreb's solution and carbogen. (Kreb's solution contains NaCl 118.1, KCl 3.4, $MgSO_4$ 0.8 KH_2PO_4 1.2, glucose 11.1, $NaHCO_3$ 25.0, $CaC_2 . 6H_2O$ 2.5 mmol/litre and has a pH of 7.4.)

The strain gauge is mounted on a Prior micrometer stage which can be moved vertically by a constant speed motor, (number 2225F0125; Portescap, UK, Ltd), at a rate of 4 mm/minute. The muscle is electrically stimulated supramaximally to ensure viability, using a Digitimer D59A stimulator set to deliver impulses at 0.2 Hz of 1 ms duration.

Laboratory diagnosis of MH susceptibility

The *in vitro* testing is carried out according to the updated European protocol[8,9] within a 5-hour time limit. Rosenberg and Reed[10] have also described a protocol for *in vitro* screening but use the caffeine contracture test only. Other workers in this field use a variety of tests, many of which have not been verified against muscle contracture tests.[11,12]

The results are classified into three diagnostic groups, MHS (susceptible), MHE (equivocal) and MHN (normal). However, the patients are told they are either susceptible to MH or normal, as the majority of the MHE group are accepted

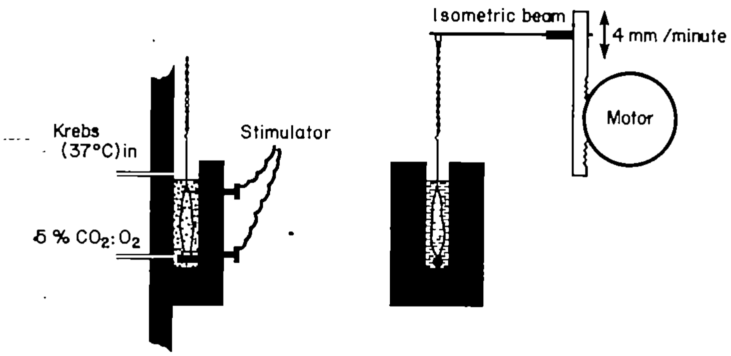

Fig. 2. A schematic diagram of the *in vitro* laboratory rig.

to be clinically susceptible and are under permanent review. In a small number of cases (see later) which cannot be clearly identified by the *in vitro* results, other factors are taken into consideration. These include CK activity, personal, clinical and family history and histological findings. The diagnosis which causes greatest concern is MHN (not susceptible to MH) and occasionally it is necessary to err on the side of caution by identifying the patient as MHS if all the results are not completely normal.

Muscle histology

The histology of muscle specimens was included as part of the muscle biopsy procedure as it was assumed that MH could be a morphological myopathy. It emerged that myopathic changes were very rare in children in the first decade, but that the percentage of abnormal biopsies increased steadily with age. The conclusion was made that the abnormalities associated with MH were not primary, but developed secondary to abnormal muscle function during the course of life. It follows that histology alone should never be used to diagnosis MH. The myopathic changes characteristic of MH are increased numbers of diffusely distributed fibres with internal nuclei, moth-eaten fibres and cores. All three abnormalities may occur in any combination. Examination of motor end plates and their innervation has shown no evidence of a neurogenic disease in MH. Electron microscopy is used to assess organelles such as the sarcoplasmic reticulum, but so far has no diagnostic significance.

Many MH investigation units do not include histology as part of the routine screening procedure. Its use is threefold, firstly to confirm a normal *in vitro* result, secondly to diagnose other myopathies which may have caused the original anaesthetic problem and lastly, as a research tool, to prove any association between MH and the various congenital myopathies.

Patient management after diagnosis

The diagnosis and its implications are fully discussed directly with the patient before discharge the following day. Patients shown to be susceptible to MH are given an application form to join the Medic-Alert Foundation, or similar organisation, which is asked to supply a disc bearing the inscription 'malignant hyperpyrexia under anaesthesia'. They are also issued with a card containing the drugs to be avoided, our address in case of emergencies and a booklet describing MH and its implications. When appropriate, further family investigations are then organised.

In 1982, the British MH Association (BMHA) was formed by a parent whose son had died from MH. The Association's aim is to help families cope with the implications of MH. The secretary of the BMHA is Mrs Alison Winks, 11, Gorse Close, Newthorpe, Nottingham.

Review of patients

Between 1971 and 1984, 1127 patients have had biopsies in this unit. The number of biopsies done each year has grown as the unit has expanded and has now reached 150–180 per year, representing four patients a week (two patients on each of two successive days) (Fig. 3). One hundred and ninety families have been identified as MHS. The yearly rate of referral of new MHS families has increased to a maximum of 28 in 1982 with a plateau of between 20–25 a year since then (Fig. 4). The number of negative probands is also increasing and, ironically, the exclusion of MH as the cause of an anaesthetic mishap is becoming an increasingly important role of *in vitro* screening. In this context, there have been 135 probands referred who have been shown not to be susceptible to MH (MHN) and on whose families further studies have not been performed.

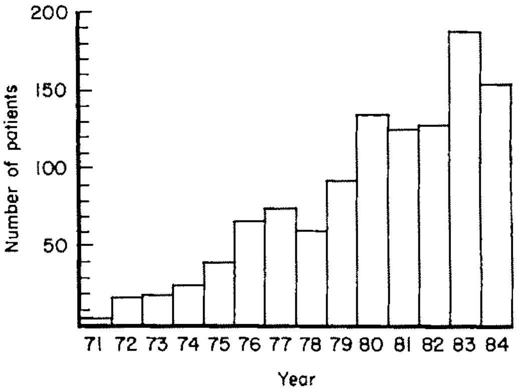

Fig. 3. Number of biopsies performed each year.

In a further 45 families the genotype has not yet been determined because the family investiga-

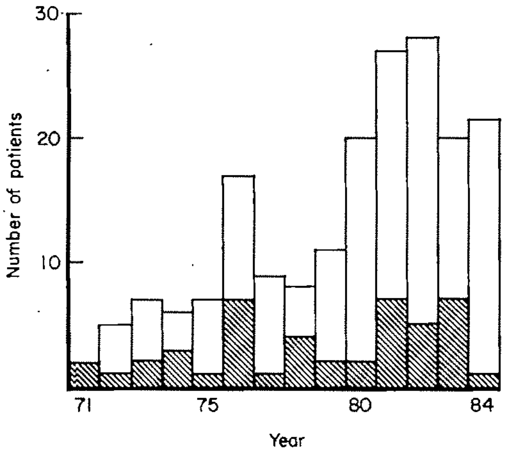

Fig. 4. Yearly referral rate of MHS probands, illustrating yearly mortality rate. □, Survived; ■, died.

tion is incomplete. Occasionally the family can never be formally proved to be MHS because clinical details are inadequate and the relevant relatives cannot be investigated. Of all the families, both positive and negative, 157 probands have not been investigated directly. These include 78 young children, 65 patients who died during the suspected reaction and 14 others, including several outside the UK. Of all patients, 480 (43%) have been shown to be susceptible to MH and 626 (55%) to be not susceptible, while 21 (2%) were inconclusive. This latter group mainly comprises children who had biopsies in the early years of the unit's activities, and it is because of these inconsistencies, possibly related to immature muscle tissue, that an arbitrary lower age limit of 10 years has been established before biopsy is undertaken. This group, however, also includes some patients in whom there is genuine difficulty in interpreting the data due to artifacts.

Since the introduction of the MHE group in 1983, 238 patients have been investigated. Sixty-four were found to be MHS, 21 MHE and 153 MHN.

The inheritance pattern of MH

The results of muscle biopsy from those patients who have a 50% chance of inheriting MH, assuming a single dominant gene, should reflect the inheritance pattern if the condition is truely autosomal dominant. The results confirm this assumption because the ratio of MHS + MHE:MHN is 353:343.

Serum creatinekinase (CK)

The use of CK as a test to predict MH was originally proposed by Isaacs and Barlow.[13] Examination of a small sample of 189 biopsied patients screened by this unit using the same blood sampling and laboratory techniques, shows a difference between the MHN and MHS population, with the MHN patients having a mean CK value of 79 (SD 57) IU/litre and the MHS patients having a mean value of 162 (SD 171) IU/litre.

Thus, as a group, the MHS patients have a significantly higher resting CK activity, although it usually falls within the normal range for this laboratory (normal <200 IU/litre). However, the large standard deviation indicates the wide scatter of the groups and the degree of overlap, thus confirming the inadequacy of the test as a screening procedure for phenotyping.[14] CK values can be used to indicate which parent to investigate initially.

MHS probands

The majority (77%) of these patients are adolescents and young adults falling into the age range 0–30 years (Fig. 5). In every instance they were apparently ASA 1 or 2 pre-operatively and death was always completely unexpected. Two thirds of the probands are male (Fig. 6), but in view of the equal distribution of MH between the sexes in the relatives who had biopsies, this pre-

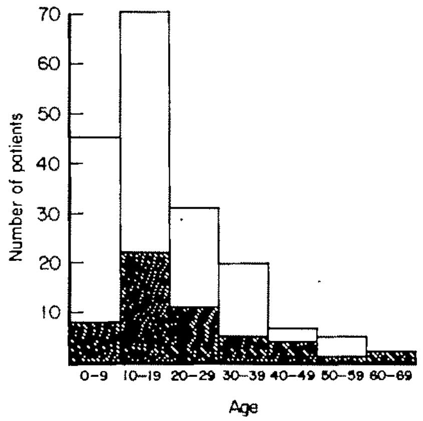

Fig. 5. Age of MHS probands, illustrating mortality rate. □, Survived; ■, died; $\chi^2 = 4.8$ ($p<0.5$).

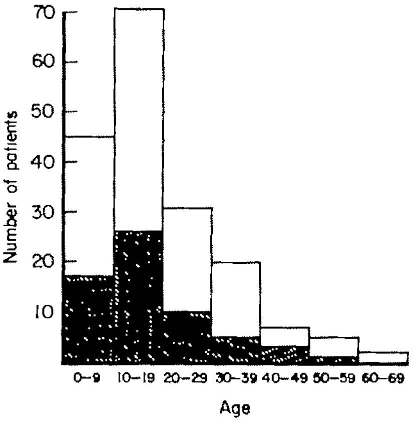

Fig. 6. Age of MHS probands, illustrating sex distribution. □, Male (68%); ■, female (32%).

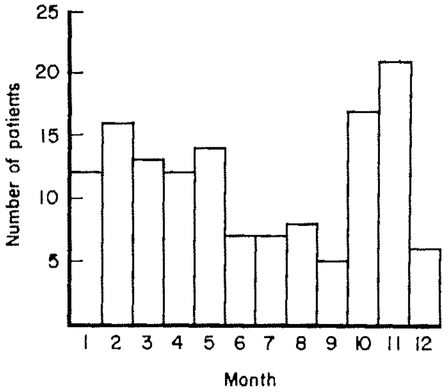

Fig. 7. The significance of the time of year on the development of MH reactions. $\chi = 23.91$ ($p<0.02$).

ponderance is seen as a reflection of differing life styles and environmental factors rather than an inherited sex-linked difference.

The mortality rate of MH was originally quoted by Britt and Kalow[15] as 68% and is now reported as being 28% in the USA.[16] This compares with an overall mortality rate in the UK, for the whole period 1971–84, of 24%, 45 of the 190 probands having died (Fig. 4). Although this incorporates a range from 100% in 1971 to 4% in 1984, using a Chi squared analysis of 3-yearly blocks, this does show a significant decrease in the mortality rate ($p<0.02$), mainly due to the low rate in 1984. Whether this follows from the introduction of dantrolene in 1980 remains to be seen, although in 1981, 1982 and 1983, also post dantrolene years, there is no evidence of this marked improvement.

Interestingly, the time of year seems to have some significant role in the development of an MH crisis (Fig. 7). Even including the seemingly low figure for December due to a major reduction in operating workload, analysis shows a significant fluctuation, with an increased incidence during the winter months ($p<0.01$).

Table 1 lists the incidence of operative procedures being performed at the time of an MH reaction. The high incidence of trauma is noticeable, but so too are the types of operations that the 0–30 year age groups tend to have, including congenital musculoskeletal problems.[17] This type of surgery often requires a type of anaesthesia most likely to trigger MH. One wonders if musculoskeletal problems are a reflection of MH or simply related to age or anaesthetic technique.

The interrelationships are made more complicated because of the existence of previous uneventful exposure to triggering anaesthetics.[18] In addition there are often subtle anthropometric differences, such as pronounced muscle development and these patients, although displaying a subclinical myopathy, often excel at sports.[19,20]

Clinical diagnosis of MH

Retrospectively, the presentation of MH is difficult to categorise because of imprecise clinical data due to inadequate anaesthetic records. Details that seem to be important in the

Table 1. Operations being performed at the time of an MH crisis

Operation	Number of cases	Percentage
Trauma	35	21.8
ENT	35	21.8
Squint/ptosis correction	13	8.3
Dental (hospital I/P)	12	7.5
Appendicectomy	12	7.5
Congenital orthopaedic	10	6.2
General surgical/genito-urinary	10	6.2
Other acute operations, e.g. abscess	7	4.4
Scoliosis	7	4.4
Congenital plastic surgery	5	3.1
Congenital hernia	4	2.5
Gynaecological	4	2.5
Orchidipexy	3	1.9
Ophthalmic	3	1.9
Totals	160	100

diagnosis of MH include a timed sequence of events involving drugs administered, the presence of muscle rigidity, blood pressure, pulse rate, core temperature, blood gases, electrolytes, initial and 24 hour CK and presence of myoglobin in the first postoperative specimen of urine.

One aspect of the presentation, namely muscle spasm with suxamethonium, has been studied.[21] This showed that 43% of MHS probands had suxamethonium spasm, of whom 11% had no other signs, 14% had minimal signs and 75% had definite signs. Other workers have also published details of the significance of masseter spasm and MH.[22,23]

We believe MH to be a specific condition which can be clearly identified by *in vitro* muscle screening tests. Studies of this group of patients should help categorise more adequately those potentially at risk. It is hoped that in the near future MH should no longer be a cause of anaesthetic death in this country.

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Ventilatory effects of propofol during induction of anaesthesia

Comparison with thiopentone

M. B. TAYLOR, R. M. GROUNDS, P. D. MULROONEY AND M. MORGAN

Summary

The ventilatory effects of induction of anaesthesia with either propofol 2.5 mg/kg or thiopentone 4.0 mg/kg have been observed in patients premedicated with either atropine alone or papaveretum and hyoscine. Induction of anaesthesia with propofol was accompanied by a greater degree of ventilatory depression which was of longer duration than following thiopentone. The effect was accentuated by the opioid premedication.

Key words

Anaesthetics, intravenous; propofol, thiopentone.
Ventilation; apnoea.

Propofol is the most recently introduced intravenous anaesthetic agent. It was originally presented in Cremophor EL and initial studies indicated that induction of anaesthesia was associated with a high incidence of apnoea.[1,2] The drug has been reformulated as an emulsion and we report here the results of an investigation into the ventilatory effects of propofol during induction, which are compared with those of thiopentone.

Methods

Studies were carried out on 80 patients of ASA grade 1, undergoing elective gynaecological surgery. All gave their informed consent to the trial which had been approved by the hospital's ethical committee. Patients who were pregnant were not studied unless the pregnancy was to be terminated by the procedure.

The patients were randomly allocated into four groups of 20 each. Forty patients received atropine only as premedication, while the remainder received papaveretum and hyoscine in the following dosage: < 50 kg, papaveretum 10 mg, hyoscine 0.2 mg; 50–70 kg, papaveretum 15 mg, hyoscine 0.3 mg; > 70 kg, papaveretum 20 mg, hyoscine 0.4 mg. The drugs were given intramuscularly 1 hour before induction, which was with either thiopentone or propofol given in a random manner.

Measurements

On arrival in the anaesthetic room, an indwelling needle was inserted into a vein on the dorsum of the hand and an Ohmeda Biox III pulse-oximeter attached to the lobe of an ear. A clip was placed on the patient's nose, and they then breathed 100% oxygen via a rubber mouthpiece from a

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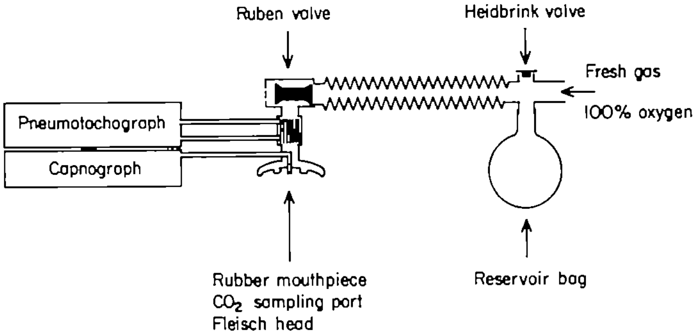

Fig. 1. Diagram of apparatus.

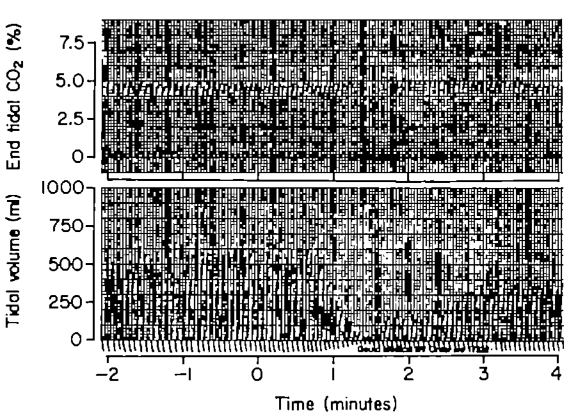

Fig. 2. Typical recording of tidal volume and end tidal CO_2. Induction of anaesthesia at time 0.

circuit shown in Fig. 1. The end tidal CO_2 concentration was recorded using a Gould Capnograph Mk III, which had been calibrated using an exact mixture of 5% CO_2 in oxygen. The expired tidal volume was measured using a Gould pneumotachograph with a Fleisch heated screen head which had been calibrated with a large syringe capable of delivering up to one litre of gas. Both breath-by-breath tidal volume and end tidal CO_2 were recorded on a hot-wire recorder; a typical trace is shown in Fig. 2.

Procedure

The patients were allowed to breathe 100% oxygen for 3–4 minutes prior to induction of anaesthesia, which was achieved with either 4 mg/kg thiopentone or 2.5 mg/kg propofol, injected over a period of 30 seconds; patients were not told when the injection began. Recordings were continued during induction and until 4 minutes had elapsed from the start of the injection or there were signs of returning consciousness. A further dose of the same induction agent was then given and anaesthesia continued with a technique appropriate to the proposed surgery.

The occurrence of any apnoea was noted and timed with a stopwatch. For the purpose of the study, significant apnoea was considered to be over 20 seconds duration. The arterial oxygen saturation was monitored by the oximeter, but not recorded and was used to assess whether ventilation required to be assisted during any period of apnoea; no such assistance was necessary in any patient.

The control mean minute volumes and respiratory rates were calculated from the trace for the 2 minutes prior to induction and then at each subsequent minute. Statistical analysis applied to the results were the paired and unpaired *t*-tests, Chi squared and Fisher's exact test.

Results

Details of the patients are shown in Table 1. Patients who received papaveretum and hyoscine and were induced with propofol were significantly ($p < 0.05$) younger and lighter than the propofol/atropine patients, and were significantly ($p < 0.05$) lighter and shorter than patients who received thiopentone and atropine. Anaesthesia was successfully induced in all patients premedicated with papaveretum and hyoscine, but in the atropine group, four given thiopentone and two who received propofol did not become unconscious. Their results are therefore not included.

The number of patients who became apnoeic are shown in Table 2. Overall, the incidence of apnoea was greater in those who were premedicated with papaveretum and hyoscine ($p < 0.05$). Up to a duration of 60 seconds, there was no significant difference in the incidence of apnoea between those induced with thiopentone or propofol. Apnoea lasting longer than 60 seconds occurred in 12 patients who received propofol (eight premedicated with papaveretum and hyoscine) compared with four who received thiopentone (two in each premedication group). This difference was significant at the 5% level. The longest apnoeic period was 240 seconds in a patient who received propofol/atropine.

The changes in respiratory rate are shown in Table 3. In patients premedicated with papaveretum and hyoscine, the fall in respiratory rate in those induced with thiopentone did not reach statistical significance, but did so in those given propofol in the first and second minutes following commencement of the injection. In both instances, the respiratory rates had almost returned to control values in the fourth minute. In the thiopentone/atropine group there was no significant fall in respiratory rate, while the fall in the propofol/atropine patients was only significant

Table 1. Demographic data of patients

	Thiopentone		Propofol	
	Papaveretum + hyoscine	Atropine	Papaveretum + hyoscine	Atropine
n	20	16	20	18
Age (years, SEM)	34.7 (2.4)	34.6 (2.7)	30.0 (1.6)	37.6 (1.84)
Weight (kg, SEM)	63.3 (2.3)	66.7 (2.07)	57.2 (2.0)	62.7 (1.61)
Height (m, SEM)	1.64 (0.01)	1.65 (0.01)	1.60 (0.02)	1.64 (0.01)

Table 2. Number of patients who became apnoeic (>20 seconds) in each group related to duration of apnoea

	Thiopentone		Propofol	
Duration of apnoea (seconds)	Papaveretum + hyoscine	Atropine	Papaveretum + hyoscine	Atropine
20–30	1	0	4	1
31–45	6	4	2	1
46–60	2	1	2	2
>60	2	2	8	4

Table 3. Mean respiratory rates (breaths/minute, SEM) in the control period and in the 4 minutes immediately following start of injection of the induction agent

	Thiopentone				Propofol			
	n	Papaveretum + hyoscine	*n*	Atropine	*n*	Papaveretum + hyposcine	*n*	Atropine
Control	20	13.3 (0.98)	16	12.4 (0.71)	20	14.7 (0.85)	18	16.5 (1.35)
1 minute	20	12.3 (1.20)	16	12.1 (0.92)	20	11.0 (1.34)*	18	10.9 (1.07)*
2 minutes	20	10.2 (1.63)	16	12.0 (1.94)	20	6.9 (1.65)†	18	12.0 (2.25)
3 minutes	19	12.0 (1.46)	13	15.3 (1.00)	20	11.2 (1.59)	13	15.3 (2.22)
4 minutes	13	11.3 (1.13)	6	15.9 (1.06)	17	12.9 (1.35)	8	16.1 (3.02)

Statistical comparison with control value (*$p < 0.05$; †$p < 0.001$). For between group comparisons, see text.

Table 4. Mean minute volumes (litres, SEM) in the control period and in the 4 minutes immediately following start of injection of the induction agent

	Thiopentone				Propofol			
	n	Papaveretum + hyoscine	*n*	Atropine	*n*	Papaveretum + hyoscine	*n*	Atropine
Control	20	6.35 (0.34)	16	5.68 (0.35)	20	6.53 (0.33)	18	7.78 (0.45)
1 minute	20	5.74 (0.45)	16	5.51 (0.44)	20	4.76 (0.57)*	18	5.23 (0.51)†
2 minutes	20	3.55 (0.17)†	16	4.28 (0.87)	20	1.61 (0.38)†	18	3.45 (0.62)†
3 minutes	19	4.78 (0.71)*	13	5.89 (0.45)	20	3.20 (0.57)†	13	5.28 (0.60)†
4 minutes	13	4.50 (0.50)*	6	6.02 (0.67)	17	4.11 (0.67)†	8	4.66 (0.86)†

Statistical comparison with control value (*$p < 0.05$; †$p < 0.01$). For between group comparisons, see text.

at one minute. Again, return to control values was rapid. Comparison between the groups premedicated with papaveretum and hyoscine revealed no significant differences in respiratory rate and, apart from the control values ($p < 0.05$), there was no difference between groups in those premedicated with atropine.

In both groups of patients premedicated with papaveretum and hyoscine, the end tidal CO_2 values were higher in the control period than in the respective patients given atropine (thiopentone 5.46, SEM 0.17 and 5.15, SEM 0.14; propofol 5.16, SEM 0.12 and 4.71, SEM 0.14). Thereafter, because of the high incidence of apnoea with consequent zero end tidal CO_2 readings, the average values obtained are not meaningful.

Table 4 shows the changes in minute volume. In patients premedicated with atropine, there was a highly significant decrease in minute volume in those induced with propofol, which lasted for 4 minutes, but the decrease associated with thiopentone induction did not reach statistical significance. Significant decreases in minute volume followed induction with both agents in those premedicated with papaveretum and hyoscine, but the degree of significance was much greater following propofol. In the atropine group, minute volumes were always lower following induction with propofol, but this was only significant in the third minute after induction ($p < 0.05$). Similarly, following papaveretum and hyoscine, the minute volumes were always lower after induction with propofol, but this was only significant in the second minute ($p < 0.05$). Following both induction agents, the minute volume was always lower in patients premedicated with papaveretum and hyoscine.

Pain on injection occurred in 12 patients induced with propofol, five of whom had been premedicated with atropine, compared to none given thiopentone. Involuntary movements in induction occurred in eight propofol patients, four in each premedication group, but were minor and of no consequence. No such movements occurred after thiopentone.

Discussion

The ideal intravenous induction agent would produce no respiratory depression. Hypoxia and hypocarbia would then not be a problem when the drug is used alone and there would be no interference with the uptake of an inhalational agent. If anaesthesia is going to be continued with a technique involving artificial ventilation, then the occurrence of respiratory depression at induction is of no consequence, although it might be important in obstetric practice, when placental transfer of the drug might have an adverse effect on the fetus, particularly those already at risk.

The present study has shown that even with the minimal induction dose, propofol has a profound ventilatory depressant effect, which is of a greater degree and longer lasting than that following thiopentone used in equipotent doses.[3] This respiratory depression was enhanced by opioid premedication. The main effect was on depth of respiration, as the rate had recovered to control values by the fourth minute after induction with both drugs.

Apnoea is a common feature of induction of anaesthesia by the intravenous route. Whitwam[4] reported an incidence of over 70% following thiopentone in patients premedicated with atropine alone, but the dose used was greater than that used here. The incidence following propofol is greater than that following induction with etomidate,[5] and the no longer available steroid anaesthetics Althesin[6] and minaxolone.[7] In a preliminary study, other workers[8] have observed a high incidence of apnoea and marked ventilatory depression following propofol 2.5 mg/kg. Profound respiratory depression was noted with the Cremophor preparation of propofol, which was accentuated by the use of premedication.[1] Fragen and his colleagues[2] also noted a high incidence of apnoea with the original preparation, although this was not significantly altered by the premedication used.

It can be concluded from the present study that induction of anaesthesia with propofol is accompanied by profound respiratory depression, which is greater than that seen following equipotent doses of thiopentone. The main virtues of propofol are the smoothness of induction, even though accompanied by an incidence of pain on injection, its ease of manipulation as a continuous infusion and the very rapid and clear headed recovery following its use in this way. The respiratory depression following a single induction dose should present no problems to anaesthetists and we agree with Goodman and colleagues[8] that it should in no way detract from the value of this new agent.

Acknowledgments

We would like to thank ICI Pharmaceuticals for the supply of propofol and Shirley Richens for secretarial assistance.

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Plasma histamine levels following atracurium

P. K. BARNES, N. DE RENZY-MARTIN, V. J. E. THOMAS AND J. WATKINS

Summary

Plasma histamine levels were determined in 41 patients, 1.5 and 4 minutes after the intravenous administration of 0.6 mg/kg of atracurium. Clinical features of histamine release were sought at the time of blood sampling. Sixteen patients had elevation of plasma histamine 2.6 (SD 1.2) ng/ml 1.5 minutes after the injection of atracurium. Plasma histamine had returned to control levels at 4 minutes. There was a poor correlation between plasma histamine levels and the clinical manifestations observed. We conclude that atracurium has a low plasma histamine release potential and that cutaneous reactions after atracurium do not always indicate that plasma histamine levels are elevated.

Key words

Neuromuscular relaxants; atracurium.
Complications; histamine release.

Experimental and clinical studies have shown that a dose-dependent release of histamine may occur following administration of neuromuscular blocking agents.[1,2] Histamine release in man has been reported following the intravenous[3] or intradermal[4] administration of atracurium besylate, a neuromuscular blocking agent of intermediate duration of action. The clinical signs following drug-induced histamine release include skin flushing and oedema with formation of wheals, cardiovascular changes and bronchospasm.[5]

Cutaneous and pulmonary signs have been reported following the administration of atracurium, but plasma histamine was not determined.[6,7] Cardiovascular changes in the form of hypotension and tachycardia have been reported to occur following atracurium if plasma histamine levels increased to 200% of control.[3]

The purpose of this study was to determine the degree of elevation of plasma histamine following the administration of atracurium 0.6 mg/kg in anaesthetised man and its correlation with clinical signs.

Methods

Informed consent was obtained from patients in the study, which had been approved by the hospital's ethical committee. The patients were fit young adults, admitted to hospital for extraction of wisdom teeth under general anaesthesia. Patients were aged between 18–35 years and had no atopic history.

Forty-one patients were premedicated with oral diazepam, 1.5–2 hours prior to anaesthesia. On arrival in the anaesthetic room, and at least 20 minutes before the induction of anaesthesia, a 16-

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gauge cannula (Abbocath) was inserted into a vein in the antecubital fossa of one arm for withdrawal of blood samples for histamine assay. A 23-gauge butterfly needle was inserted into a vein on the dorsum of the opposite hand and was used for drug administration. One minute before the induction of anaesthesia, 10 ml of blood were withdrawn into a Sarstedt syringe (sample 1). Following induction with thiopentone 0.5 mg/kg, patients breathed a mixture of 70% nitrous oxide in oxygen from a Mapleson C system. After 4 minutes, a second blood sample was taken, (sample 2). One minute later, atracurium 0.6 mg/kg was administered over 5 seconds. When spontaneous ventilation ceased, the lungs were ventilated with the same mixture of nitrous oxide and oxygen via a facemask. Further blood samples were taken 1.5 minutes (sample 3) and 4 minutes (sample 4) after the administration of atracurium. Blood samples were immediately placed under ice and centrifuged within the hour. Histamine levels in plasma were measured by the fluorometric method described by Lorenz.[3] Mean arterial blood pressure and heart rate were measured using an automatic blood pressure monitor (EME). Measurements were made before induction of anaesthesia and then each time blood was sampled. Following the administration of atracurium, any cutaneous signs suggestive of histamine release were noted and graded as either minimal, moderate or severe. Correlation coefficients were calculated for elevations in plasma histamine and the absolute changes in mean blood pressure and heart rate at 1.5 minutes following atracurium administration.

Results

Plasma histamine levels

Control values of plasma histamine among patients ranged from 0.2–0.5 ng/ml (sample 1). Subsequent elevations in plasma histamine were expressed in ng/ml above control values. An increase in plasma histamine was found in 16 of the 41 patients in the sample taken 1.5 minutes after the administration of atracurium (sample 3). Levels ranged from 0.5–5 ng/ml above control, mean 2.6 ng/ml (Fig. 1). In these patients, plasma histamine levels were approaching control values by 4 minutes. Four patients showed increases in plasma histamine following thiopentone (sample 2). The levels ranged from 0.3–1.5 ng/ml above control values. In addition, two patients had no increase in plasma histamine in sample 3 but did develop minimal increases in sample 4 (0.25 and 0.35 ng/ml).

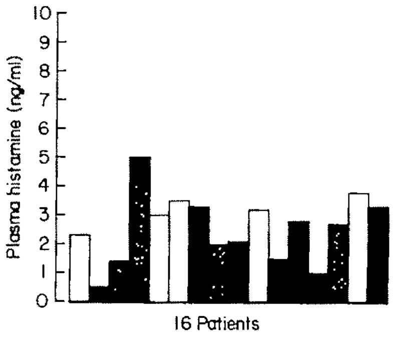

Fig. 1. Plasma histamine levels in 16 patients. ▨, Severe skin flush; ■, mild to moderate skin flush; ☐, no skin flush.

Cutaneous signs

Cutaneous signs following atracurium occurred in 23 of the 41 patients. They appeared within 1.5–2 minutes after injection, had usually disappeared within 5 minutes and were manifested as a skin flush over the upper trunk and neck. This was graded as minimal in 13 and moderate or severe in 10. Elevation in plasma histamine was detected in five of the 13 patients with minimal skin flushing and six of the 10 patients with moderate or severe skin flushing, (Fig. 1). One patient with severe skin flushing also developed two wheals on the upper arm. Five patients who had elevated plasma histamine levels did not show any cutaneous manifestations. Twelve patients who developed skin flushing did not have elevated plasma histamine levels.

Mean blood pressure

Mean blood pressure 1.5 minutes after the injection of atracurium was compared with control values 4 minutes after injection of thiopentone. Nine patients experienced a fall in mean blood pressure greater than 10% of control. Of these, five had increases in plasma histamine, (Fig. 2). There was no correlation between plasma histamine and decrease in mean blood pressure, ($r = 0.33$).

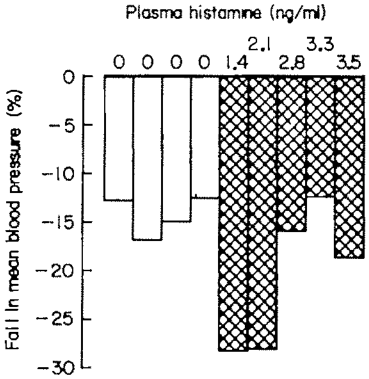

Fig. 2. Nine patients with fall in mean blood pressure 1.5 minutes after atracurium of greater than 10% control and their associated plasma histamine levels. □, No increase in plasma histamine; ▨, elevation in plasma histamine.

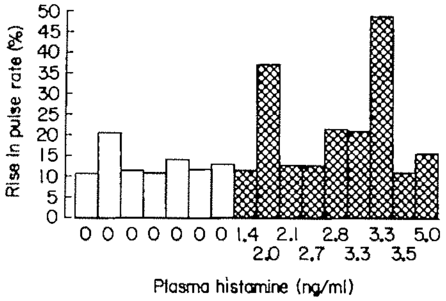

Fig. 3. Sixteen patients with elevation in pulse rate 1.5 minutes after atracurium of greater than 10% of control and their associated plasma histamine levels. □, No increase in plasma histamine; ▨, elevation in plasma histamine.

Mean heart rate

After the administration of atracurium, an increase in heart rate occurred in 26 patients. In 16 patients the increase was greater than 10% of control values. Of those 16 patients, nine had elevations in plasma histamine level, (Fig. 3). There was no correlation between the plasma histamine and the change in heart rate, ($r = 0.14$).

Bronchospasm

None of the patients in this study developed any evidence of bronchospasm.

Discussion

Control values for plasma histamine in all subjects in this study were in the range 0.2–0.5 ng/ml, which is consistent with previously published work.[9] The major change in plasma histamine was detected in the blood sample taken 1.5 minutes after the administration of atracurium. Elevation of plasma histamine occurred in 39% of subjects at this time. The levels of plasma histamine reported in this paper are well below the threshold of 12 ng/ml that Lorenz[10] considers necessary for severe clinical sequelae. Four patients had elevations in plasma histamine following thiopentone (levels ranged from 0.3–1.5 ng/ml). In addition, two patients had no increase in plasma histamine 1.5 minutes after the injection of atracurium but had minimal increases in the sample taken 4 minutes after the injection. As these plasma histamines were only 0.25 ng/ml and 0.35 ng/ml, they have not been represented in the figures. The marked variability in the peak plasma histamine following atracurium found in this study has also been noted with tubocurarine[2] and morphine.[11]

Despite the significant variability in tubocurarine histamine release, a positive correlation with observed hypotension was described by Moss *et al.*[2] who also found that the dose of atracurium that produced a 200% increase in plasma histamine above control (0.6 ng/ml) resulted in a significant fall in blood pressure and an increase in heart rate.[3] In the present study, the majority of patients who had a fall in mean blood pressure of greater than 10% of control or an increase in heart rate of greater than 10% of control, had evidence of systemic histamine release. However, changes in these parameters did not correlate with peak plasma histamine levels. The differences in these results compared with previous studies may be attributable to the different protocols used or the different populations examined.

Cutaneous reactions in the form of skin flushing and wheals have been reported by several authors after the administration of atracurium in doses ranging from 0.3–0.6 mg/kg.[12,13] The incidence of cutaneous reactions vary in the reports from 10–75%. In the present study, we observed skin reactions in 56% of subjects given a large dose of atracurium. Twenty-three subjects developed skin flushing, but elevation in plasma histamine was detected in only 11. A similar finding has been reported with morphine, by Rosow *et al.*,[14] who found that prominent itching and skin flushing could occur without changes in plasma histamine. We consider that histamine release may occur in the skin in a proportion of patients without detectable levels in the blood stream.

We conclude that atracurium has a lower potential for histamine release than tubocurarine and that the clinical signs of histamine release correlate poorly with plasma histamine levels. The mechanism of histamine release following atracurium is an area for further study.

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Anaesthesia, 1986, Volume 41, pages 825–828

Ventilation and the oculocardiac reflex

Prevention of oculocardiac reflex during surgery for squints: role of controlled ventilation and anticholinergic drugs

R. K. MIRAKHUR, W. F. I. SHEPHERD AND C. J. JONES

Summary

A randomised prospective study was carried out in children undergoing surgery for squint correction, to determine the value of controlled ventilation as a prophylaxis against the occurrence of the oculocardiac reflex. One hundred patients anaesthetised with nitrous oxide/oxygen and halothane were randomly assigned to either ventilated or spontaneously breathing groups of 50 each. Half the patients in each group received glycopyrronium 7.5 µg/kg intravenously at the time of induction of anaesthesia. Heart rate, rhythm, blood pressure and end tidal CO_2 *concentration were monitored throughout. A positive oculocardiac reflex, defined as a fall in heart rate of 20% or more and/or the occurrence of dysrhythmias, was observed in 72% of spontaneously breathing patients and in 100% of ventilated patients not receiving prophylactic intravenous glycopyrronium. The incidence of a positive reflex in patients receiving glycopyrronium was 10% (4 and 16% respectively in spontaneously breathing and ventilated patients). It is concluded that controlled ventilation is of no value as a preventive measure against the occurrence of the oculocardiac reflex in patients undergoing squint surgery and that prophylaxis is safely achieved with the use of intravenous glycopyrronium.*

Key words

Anaesthesia; paediatric, ophthalmic.
Complications; oculocardiac reflex.

The oculocardiac reflex is a common occurrence in ophthalmic surgery and is frequently observed in children undergoing correction of squints.[1,2] It has previously been shown that intravenously administered anticholinergic drugs, such as atropine and glycopyrronium, are effective in preventing its occurrence; the latter does so without producing excessive tachycardia.[2] A previous study in spontaneously breathing children[3] showed that the reflex was evoked less frequently in those whose $Paco_2$ had been normal or low; however, this study did not include for comparison a group of patients who were ventilated. A small prospective study,[4] on the other hand, showed that the incidence of the oculocardiac reflex was similar in children, irrespective of whether their ventilation was controlled or spontaneous. This study, however, did not include a group receiving anticholinergic prophylaxis; consequently, the incidence of the oculocardiac reflex was high in both groups.

The present study was designed to investigate, prospectively, the influence of both controlled ventilation and anticholinergic drug therapy on

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the occurrence of the oculocardiac reflex in children.

Methods

Children aged 1–14 years, undergoing surgery for the correction of squints, were included in the study after obtaining approval from the regional ethics committee. They were premedicated with oral trimeprazine 2 mg/kg 2 hours before anaesthesia and were divided into two main groups, those breathing spontaneously and those being ventilated. Within each group, half the patients received intravenous glycopyrronium 7.5 µg/kg, half received an inert preparation. The allotment of patients to the four subgroups was according to a computer-generated randomisation scheme. Anaesthesia was induced with 2.5% thiopentone 5–6 mg/kg intravenously or by inhalation of nitrous oxide/oxygen and halothane. Glycopyrronium or placebo were administered 5 minutes before, or soon after induction of anaesthesia. Those breathing spontaneously were intubated using suxamethonium 1 mg/kg, those being ventilated received vecuronium in an initial dose of 0.1 mg/kg, supplemented by further small increments when necessary. Vecuronium was chosen as the muscle relaxant in ventilated patients, both for its relatively short duration of action appropriate for this type of surgery, and for the absence of tachycardia[5] following its administration. Anaesthesia was maintained with 60% nitrous oxide in oxygen and halothane 1–2%. All patients received pethidine 0.5 mg/kg intravenously soon after induction of anaesthesia. Residual neuromuscular block was antagonised in ventilated patients with neostigmine 0.05 mg/kg and glycopyrronium 0.01 mg/kg.

Heart rate and rhythm and blood pressure were continuously monitored and ECG recordings made prior to and during application of traction to the extra-ocular muscles and at any other time if an abnormality was noted. End tidal CO_2 was continuously measured throughout the procedure.

A T-piece system was used for those patients who breathed spontaneously with a fresh gas flow rate of up to three times their calculated minute volume. Controlled ventilation was carried out using an Engström ventilator and a non-rebreathing system, and was adjusted to maintain an end tidal CO_2 concentration between 4.5 and 5.0%.

The oculocardiac reflex was defined as a fall in heart rate of 20% or more and/or the development of dysrhythmias as a result of traction on the extra-ocular muscles (as used in previous studies[2,4]). Traction on the extra-ocular muscles was temporarily released and intravenous glycopyrronium 0.1–0.2 mg administered if the heart rate fell to less than 70 beats/minute.

Statistical analysis of the results was carried out using an analysis of variance; if this showed a significant 'group' effect, further analysis was carried out using two sample *t*-tests on parametric data and a Chi squared test on non-parametric data.

Results

A total of 100 children were included in the study and were assigned to four subgroups of 25 each as follows: group 1, spontaneously breathing and receiving glycopyrronium; group 2, spontaneously breathing, but not receiving glycopyrronium; group 3, those being ventilated and receiving glycopyrronium; group 4, those being ventilated, but not receiving glycopyrronium.

The comparability of the groups with regard to the ages and weights of the patients, heart rates before traction of the first muscle and the

Table 1. Demographic data

	Spontaneous ventilation		Controlled ventilation	
	Group 1	Group 2	Group 3	Group 4
Number receiving intravenous induction	16	18	21	16
Number receiving inhalational induction	9	7	4	9
Age (years, SEM)	5.4 (0.5)	6.0 (0.8)	6.8 (0.6)	5.8 (0.7)
Weight (kg, SEM)	19.8 (1.3)	22.4 (1.8)	22.9 (1.6)	20.9 (1.7)
Heart rate before traction (beats/minute, SEM)	142 (2.5)	107 (4.0)	146 (3.4)	114 (3.8)
Number showing a positive oculocardiac reflex (%)	1 (4)	18 (72)	4 (16)	25 (100)
End tidal CO_2 concentration (mean percentage, SEM)	6.5 (0.16)	6.5 (0.25)	4.7 (0.12)	4.4 (0.10)

Table 2. Frequency and mode of presentation of oculocardiac reflex

	Spontaneous ventilation		Controlled ventilation	
	Group 1	Group 2	Group 3	Group 4
Oculocardiac reflex: *n*(%)	1 (4)	18 (72)	4 (16)	25 (100)
Fall in heart rate of 20% or more: *n*(%)	1 (4)	15 (60)	3 (12)	24 (96)
Dysrhythmias: *n*(%)	0	11 (44)	2 (8)	20 (80)

Some patients exhibited both a fall in heart rate and dysrhythmias.

end tidal CO_2 concentrations, are given in Table 1. The distribution of intravenous or inhalational inductions was similar amongst the four subgroups. The ages and weights were comparable, with no significant differences between the groups. Analysis of variance showed a significant difference ($p < 0.01$) in heart rates between the groups. Further analysis using two sample *t*-tests showed the heart rates in groups 1 and 3, i.e. those given intravenous glycopyrronium, to be significantly higher ($p < 0.001$) than those in group 2 and 4 respectively. At the same time, the heart rates in groups 1 and 3 and groups 2 and 4 were not significantly different from each other. As expected, the average end tidal CO_2 concentration in spontaneously breathing patients was significantly higher ($p < 0.0001$) than in those whose ventilation was controlled.

The incidence of the oculocardiac reflex which varied from 4 to 100% in various groups is shown in Table 2. A Chi squared analysis showed the difference between the groups to be significant (Chi squared = 62.5, dof 3, $p < 0.0005$). It is clear that controlled ventilation, *per se* (group 4) was not associated with a lower incidence of oculocardiac reflex; in fact, this group had the highest incidence (100%). Within each of the two main groups, administration of glycopyrronium resulted in a highly significant reduction ($p < 0.0005$) in the incidence of oculocardiac reflex, irrespective of the mode of ventilation. The overall incidence was reduced from 86% (groups 2 and 4 combined) to 10% (groups 1 and 3 combined).

Table 2 also shows the manifestations of the oculocardiac reflex. It is clear that dysrhythmias are a frequent accompaniment of significant falls in heart rate during traction on the extra-ocular muscles. The most common dysrhythmia noted was nodal rhythm. In addition, frequent ventricular ectopic beats were observed in two patients in group 2 and sinus arrest of 2.8 and 3.6 seconds in two patients in group 4. Fourteen patients were given intravenous glycopyrronium for falls in heart rate to below 70 beats/minute associated with traction; this resulted in multiple ventricular ectopic beats in one patient. One patient each given glycopyrronium prior to induction of anaesthesia developed occasional ventricular ectopic beats and accelerated junctional rhythm respectively.

Discussion

Various prophylactic measures have been advocated for the prevention of the oculocardiac reflex. These have included retrobulbar block,[6] the use of gallamine,[7] artificial ventilation[8] and the intravenous use of anticholinergic drugs.[1,2,9]

Retrobulbar block and the use of gallamine have not proved popular since, by themselves these do not provide adequate protection or are associated with complications. There are conflicting views on the role of artificial ventilation. Over 20 years ago, Aserinsky and Debias,[8] on the basis of their experimental work in dogs, suggested its use for the prophylaxis of the oculocardiac reflex and recently its use was supported by Blanc and his colleagues.[3] Forestner and Imbrecht,[4] on the other hand, were unable to show any benefit from artificially ventilating their patients, and the results from the present study support their findings. However, both Aserinsky and Debias[8] and Blanc *et al.*[3] did not actually employ artificial ventilation in their studies. Aserinsky and Debias[8] kept their dogs apnoeic after a period of intense hyperventilation, presuming the CO_2 to be low but without actually measuring it. In the study by Blanc *et al.*,[3] efficient ventilation was defined as normal or low $Paco_2$ in spontaneously breathing children. Moreover, they defined a positive oculocardiac reflex as a fall in heart rate of 7.5 beats/minute, a fall that is perhaps of very small consequence in contrast to a realistic and clinically important fall in heart rate of 20% or greater or the development of dysrhythmias as used by us in the present study and previously by ourselves and others.[2,4]

The present study confirmed artificial ventilation, associated with a significantly lower end tidal CO_2 concentration, to be of no prophylactic value. Glycopyrronium administration was necessary to reduce the incidence of the oculocardiac reflex in the ventilated patients. Even then, the results were similar to those obtained with the use of intravenous glycopyrronium in those breathing spontaneously and with a significantly higher end tidal CO_2 concentration. In the only study[10] where artificial ventilation and the use of the anticholinergic drug atropine were compared for the prevention of the oculocardiac reflex, the authors showed that, whereas controlled ventilation prevented the oculocardiac reflex almost completely in dogs, it was not as effective in humans, in whom intravenous atropine was the most effective. A 35% incidence of dysrhythmias was, however, reported in this study in patients given atropine, but not all the dysrhythmias were observed in children and in many cases these were observed during procedures such as tracheal intubation. Studies concerning the use of intravenous atropine and glycopyrronium in children[11,12] awake or anaesthetised with halothane, showed no serious dysrhythmias. Transitory, accelerated junctional rhythm, unaccompanied by any significant changes in blood pressure, was the most common.

Glycopyrronium was chosen in the present study since it was shown in earlier studies[2,9] to provide adequate protection against the oculocardiac reflex, without producing excessive tachycardia or excessive dysrhythmias. In addition, it has a better antisialogogue action and its effects are longer lasting.[13]

In conclusion, the present study shows that controlled ventilation in itself does not provide any protection against the oculocardiac reflex and that anticholinergic drug administration is the more effective prophylaxis.

Acknowledgments

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HISTORICAL

Nikolai Ivanovich Pirogoff

O. SECHER

Summary

A short description of the life of Nikolai Ivanovich Pirogoff and some of his accomplishments are given. His book on administration of ether for anaesthesia (analgesia) by inhalation and by rectum is of special interest. In this book he also describes his experiments, mainly on dogs, with all kinds of administration. He was one of the first to write a book on ether and also to utilise anaesthesia under war conditions. Later he tended to favour chloroform, which he considered to be better. He accomplished a lot in life and was highly regarded at home and abroad.

Key words

History; Pirogoff, Nikolai Ivanovich.

The name of Nikolai Ivanovich Pirogoff (Pirogov), 1810–81, is well known in the history of anaesthesia and is mainly connected with the rectal administration of ether vapour. Rarely mentioned, however, is his book[1] on the use of ether entitled *Recherches pratiques et physiologiques sur l'éthérisation*, published in St Petersburg in 1847, and which was one of the first on the subject.

Before Pirogoff published his book, at the end of May or early June 1847, (it was approved by the censor on the 17th of May 1847) a short message which he sent to the Academie des Sciences in Paris, was presented at its meeting on the 5th of May 1847. This was entitled *'Nouveau procédé pour produir, au moyen de la vapour d'éther, l'insensibilité chez les individus soumis a des opérations chirurgicals'*.[2] After having experimented with dogs he had used rectal administration of ether vapour on patients with good results.[3–5] On 16th March, 1847, Marc Dupuy, an interne de hôpitaux at the Hotel Dieu in Paris, had presented a similar paper at the Academie de Médicine, but no abstract of this paper exists. Three weeks later, Dupuy presented his results to the Academie des Sciences: *'Note sur les effects de l'injection de l'éther dans le rectum'*. He had experimented with three dogs and a rabbit and injected a mixture of 15 g ether and 15 g water into the rectum. He found his results better than ether administered by inhalation.[4–6] The same year, Marc Dupuy published a book: *De l'éthérisation* but this has not been seen by the author of the present article.

Shortly after the appearance of his book, Pirogoff sent a copy to the Academie, together with another message which was read to the Academie at the meeting on the 21st of June. *'Effects des vapeurs d'éther par la rectum'*. In this he mentioned that he had used 'his method' on seven more patients. This presentation has been published.[4,5,7] In his comments on this presenta-

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tion, W. Stanley Sykes (1894–1961) states: 'Here, as in the case of Velpeau (Louis Velpeau, 1795–1867, Charrité, Paris) we can trace the beginning of the continental attitude to anaesthesia. If things do not work perfectly the first time, do not bother to learn how to do it. There is not anything to learn. Try something else'.[5] This is not a fair statement, and can only be due to the fact that Sykes had not read Pirogoff's book. Sykes also states that Pirogoff first gave rectal ether on 2 April, 1847, but I have not been able to confirm this. Pirogoff was convinced that he had found a better method for the administration of ether, which gave less trouble to the patient and the surgeon.

Although Pirogoff must be considered the first to have administered ether per rectum to patients, neither he nor Dupuy were the first to experiment with the method. J. Vincente y Hédo in Madrid had tried it on animals, but considered it too dangerous.[8,9] Also, the Austrian veterinarian, H. Seifert, had used it and gave a demonstration of it on horses, cows, sheep and dogs on the 6 February 1847.[8] In his book Pirogoff mentions only one name, Magendie (Francois Magendie, 1783–1855) who had performed experiments on animals using rectal ether, but clinicians had paid no attention to it. Perhaps it was Magendie who gave Pirogoff the idea.

Education and career

It is pertinent to record briefly the life and accomplishments of Nikolai Ivanovich Pirogoff (Fig. 1). He was born in Moscow on the 13 November 1810, the son of a treasurer and he had his first schooling and first medical education there. He graduated from the University in 1827 at the age of 16 years. The same year he was selected as a crown stipendiary and sent to the University in Dorpat for further training. Here the education was better, and the students were selected likely candidates for the future position of professor. He graduated in 1832 and defended his thesis the same year: *Num vinctura aortæ abdominalis in aneurysmate inguinali adhibita facile ac tutum sit remedium?* (Is the ligation of the abdominal aorta in inguinal aneurysm an easy and safe procedure?).

The University of Dorpat (Fig. 2) was founded in 1626 by the Swedes under King Gustav II Adolf (1594–1611–1632), and named Academia Gustavianum, as Estonia at that time was a Swedish area. The university got the same privileges as the university in Uppsala, founded in 1477. It functioned until 1656 when the Russians conquered the city, but was re-established in 1690 under King Carl XI (1655–1660–1697) and given the name Academia Gustavo-Carolina. In 1699 it was moved to Pernau (Pärnu), as the Russians once more conquered the city. During the war between King Carl XII (1682–1697–1718) and Emperor Peter the Great (1672–1682–1725) Sweden lost Estonia in 1710 and the university was closed.[10] In 1802 it was re-opened by the Russians under Emperor Alexander I (1777–1801–1825) in Dorpat (Tartu), this time with a heavy German influence, and it

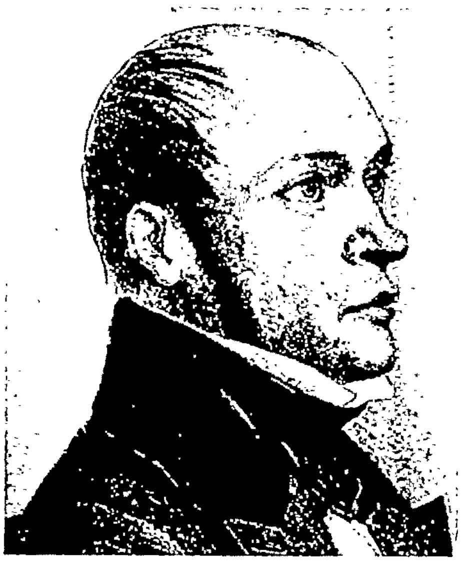

Fig. 1. Nikolai Ivanovich Pirogoff at the time of his graduation from Dorpat.

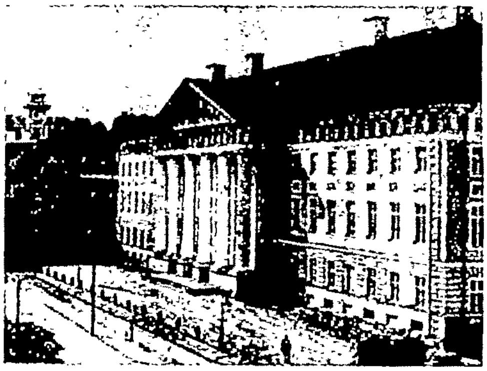

Fig. 2. University of Dorpat.

still exists. In the same period, the Swedes also founded a university in Åbo (Turku) in 1640 and in Lund in 1666. They had taken over the university in Greifwald, founded in 1456, when Pommern belonged to Sweden from 1630 to 1720.

During his studies in Dorpat, Pirogoff concentrated on anatomy and surgery, two subjects which were to be his main interest in the following years. In 1833 the crown stipendiaries were sent to Germany for 2 years for further education. Pirogoff decided to go to Berlin via Copenhagen and Hamburg. He went to Copenhagen by ship from Riga and this was the first city he visited outside Russia. Here he visited hospitals and was well received by the surgeons, except for one, who refused to allow him to observe his operations. The surgeon was a well known cystoscopist, Ludwig Lewin Jacobson (1783–1843), who had invented a cystoscope for stone crushing. Unfortunately, Pirogoff does not write very much more about his visit.[11]

He studied surgery for 2 years in Berlin and Göttingen and returned to Russia in 1835. The following year, Pirogoff became professor of surgery at the Dorpat University until he moved to St Petersburg in 1841. His wish had been to become professor in Moscow. Apart from visiting Paris and Germany in 1837–38, he devoted his time at Dorpat to surgery, anatomical studies and teaching. During this period he wrote a number of articles and two monographs: *Über die Durchschneidung der Achilles-Sehne als operativorthopädisches Hilfmittel*, Dorpat 1840 (About the cutting of the Achilles tendon as an operative orthopaedic help) and *Chirurgische Anatomie der Arterien und der Fascien*, Dorpat 1840 (Surgical anatomy of the arteries and fasciae).

Shortly after his promotion to professor at the Military Medico-Surgical Academy in St Petersburg (Fig. 3), he married a daughter of count Dimitri Berjosin, and the year after they had a son and 2 years later another. Shortly after the last delivery his wife died of a meningitis. Later he remarried, before the Crimean War. His oldest son, Nicolaj Nicolajewitsch Pirogoff (1843–91) became a known physicist.

Pirogoff's stay in St Petersburg (Fig. 4) lasted until 1860, and here he made considerable improvements in the hospital, organised operations and continued his anatomical and surgical studies. When the Danish doctor Peter Plum (1829–1915), later professor of surgery, visited the hospital in 1866–67, he gave a very favourable description of it, but he never met Pirogoff, who had retired by that time.[12]

Fig. 3. Pirogoff at the time when he was professor of surgery at St Petersburg.

Pirogoff's anatomical studies, which he started in Dorpat, finished with the issue of a great atlas in 1849: *Anatomia topographica sectionibus per corpus humanum congelatum triplici directione ductus illustrata.* This consisted of four volumes with 224 drawings of typographical anatomy of sections in three directions through the frozen human body. He published a further book *Chirurgische Anatomie der Arteriestamme etc.* in 1860.

Researches in anaesthesia

He started his investigations on ether early patient on the 14 February.[13] He must have started his animal experiments shortly after. In his book: *Recherches pratiques et physiologiques sur l'éthérisation** (Fig. 5), he described his

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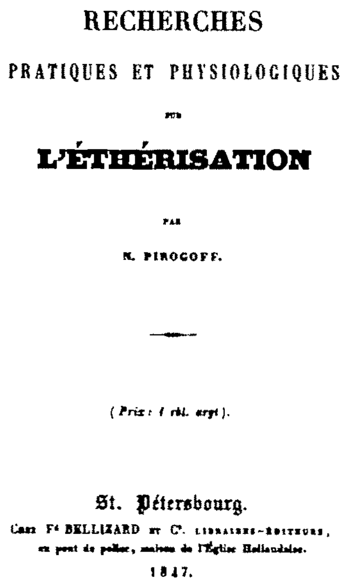
*Professor Elena Damir, Moscow, has informed me that only one copy of this book exists in Russia, namely at the library of Leningrad, where it is safely locked up.

Fig. 4. Military Medico-Surgical Academy, St Petersburg.



RECHERCHES

PRATIQUES ET PHYSIOLOGIQUES

SUR

L'ÉTHÉRISATION

PAR

N. PIROGOFF.

(*Prix : 1 rbl. argt*).

St. Pétersbourg.

Chez Fd BELLIZARD et Co. LIBRAIRES-ÉDITEURS,
au pont de police, maison de l'Église Hollandaise.
1847.

Fig. 5. Front page of Pirogoff's book on researches with ether, published in 1847.

experience of administering ether to 50 patients and 40 volunteers. Initially, he used a primitive apparatus, a bottle with a tube to the nose and a Charrière apparatus (Joseph Frederic Benoit Charrière, 1803–76, a Paris instrument maker).[14] Pirogoff was not satisfied with this apparatus, as the mask was too small and the resistance too high, so he constructed an apparatus of his own for ether inhalation (Fig. 6).

He summarised his experiences in the following statements: 'even if the inhalation of ether is indicated in all important and painful operations, its action on muscle-function cannot be predicted. A pre-anaesthetic test cannot alone predict this, but will make the patient more confident; for operations that are delicate rather than painful ether should not be used because of excitation, convulsions and automatic movements; in eye operations it can make circumstances easier as well as more cumbersome; it should not be used for operations in the mouth and pharynx; for stone crushing it is as useful as for other operations; removing stones through loin or perineum is much easier due to muscle relaxation. In deliveries, rupture of the perineum is avoidable. However, it can provoke urinary bladder spasms; above all etherisation is useful for incarcerated hernias, dislocations and ankyloses, because of its relaxing effect on the muscles; experience shows that ether inhalation should never be used on patients with dispositions for haemoptysis and headaches; for therapeutic purposes, ether can be mixed with other substances which are soluble in ether.'

The next part of the book is an account of his experiments mainly on dogs. He started by applying ether directly to peripheral nerves, the medulla and brain, while stimulating the areas mechanically and electrically. In another series, he administered ether intravenously and intra-arterially and thereafter stimulated peripheral nerves. In some of the experiments he gave ether as a vapour. For arterial injection he used carotid and crural arteries. In single experiments ether was given into the portal vein and the stomach.

In the third series, ether was given trans-tracheally, and the 'pneumogastric' nerve was

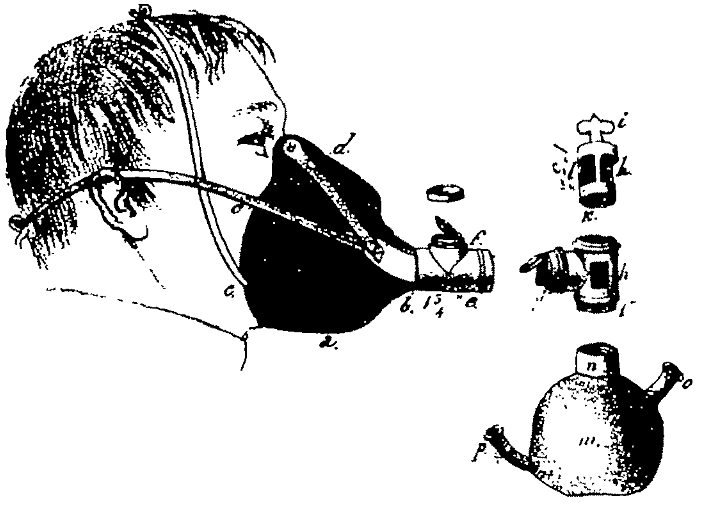


Fig. 6. Illustration of Pirogoff's mask and apparatus for inhalation of ether, taken from his book. There is an inspiratory/expiratory valve and a mechanism to adjust the concentration of ether. The ether chamber was kept reasonably small and was made of metal to ensure vaporisation.

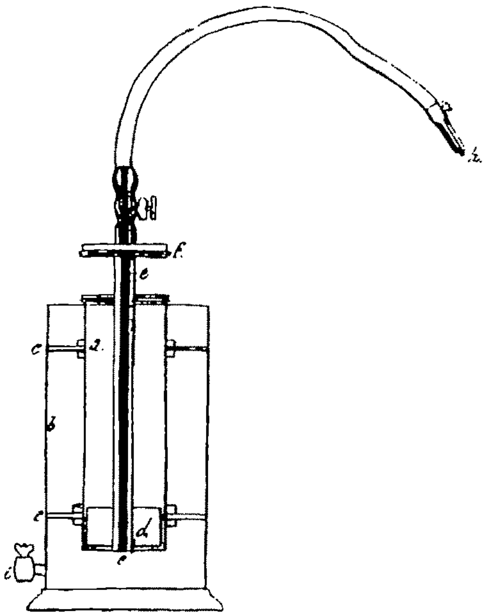


Fig. 7. Illustration of Pirogoff's apparatus for rectal administration of ether vapour, taken from his book. It consists of a syringe surrounded by a metal cylinder filled with water at 50–62°C. f is the cover of the syringe, d the piston and ee is a hollow rod. Ether is poured into the cylinder of the syringe, the piston placed in position and the syringe closed. The ether vapour passes through the rod into the flexible tube h, which is inserted into the patient.

cut, after which the effects of stimulation of the peripheral nerves was examined. In a couple of experiments the effect of ether was compared with ammonia, and also the effect of strychnine on the medulla was tested. One dog had a Caesarean section with the aid of ether, but the four puppies died.

The fourth group of experiments concerned the rectal administration of ether vapour. In a couple of experiments the rectum was ligated before the administration, and in a single case the thorax was opened and the irritability of the heart examined. Shortly after the rectal administration it was possible to smell ether in the expired air.

To obtain anaesthesia two conditions had to be fulfilled: ether had to be absorbed in the blood mass and there had to be contact between the blood and the nervous system. After these experiments he gave a long explanation of the results obtained. If liquid ether is injected into a vein, death occurs immediately, even if the vein is not close to the heart. The same result is obtained if it is injected into the carotid artery. The first case he likened to an air embolism; the second case, he suggested, was similar to increased intracranial pressure. Animals can be anaesthetised by careful injection of ether vapour, but if it is mixed with air the animal will die.

Signs of anaesthesia are only seen when etherised blood has passed the lungs. The smell of ether in the expired air is therefore an important sign of sleep and loss of pain sensation and indicates that ether has passed from the lungs into the arterial blood. Rectal administration of ether results in rapid absorption due to the large surface. He concluded that ether had a limited local action on nerves and when applied directly to the brain, anaesthesia was not efficient until it could be smelled in the expired air. This meant that ether had passed into the blood through open veins, dura mater and brain nerves.

After this Pirogoff established four degrees of anaesthesia: *1st degree:* as long as ether is present only in venous blood, or as long as the arterial blood is not sufficiently saturated with ether, etherisation only influences the circulation and the respiratory organs; *2nd degree:* here the brain is affected, but not the medulla motor or sensory fibres; *3rd degree:* this is a higher degree of influence on the medulla, reflexes disappear, mechanical stimulation of the nerves has no effect, but galvanic stimulation still works and can produce convulsions; *4th degree:* no sensation or movements and total relaxation. Irritation of medulla has no or reduced action and only the heart is beating.

In the last part of the book he gives instruction on the rectal administration of ether and a description of his apparatus (Fig. 7). He regarded this method as superior to inhalation as there was no excitement, anaesthesia was induced rapidly following removal of the apparatus and muscle relaxation was better. Other advantages he claimed were that the respiratory organs were not affected, the method was independent of the patients will, there was no excitation, so that the patient appeared to be in a deep sleep; which was important during serious and delicate operations, and it lasted longer.

Following this, Pirogoff went on to describe his experiences with operations on 50 patients using ether anaesthesia. In six or seven, etherisation by inhalation was not successful, either due to defects in the apparatus or because the patients had had too little ether before the operation started. Using rectal ether in 40 cases, one was unsuccessful because the rectum was full, in another the construction of the flexible tube from the vaporisation chamber was faulty, while in a third the rectum was too irritable. Two patients died due to renal disease. He noted that the fever reaction was limited, especially after amputations, herniotomies and removal of large tumours. He stated that it was too early to give an opinion of 'my method' because it had been used on an insufficient number of cases and also that one day it could be expected that the use of ether either through the lungs, rectum or skin would have a beneficial effect on internal and external diseases.

He concluded that because of the advantages of his method of rectal ether, it was to be preferred in the following cases: all delicate, painful and long lasting operations; all obstetrical operations; operations which need muscle relaxation, reposition of incarcerated hernias and dislocations; spasmodic diseases in guts and urinary organs and spastic diseases in voluntary muscles. Because of the perfect muscle relaxation, which is seen following rectal administration, this method is suggested in these cases.

Shortly after Pirogoff finished his book, he had a chance to use ether for anaesthesia under war conditions. In the beginning of spring 1847, mountain tribes in the Caucasus area rebelled against the Russian government, and in the beginning of June Pirogoff was ordered to travel to the war area. He arrived in Piatigorsk at the end of June, where he treated the first wounded. For anaesthesia he had brought with him a number (?30) of his anaesthesia masks.[13] Being a director of a factory manufacturing surgical equipment, this must have been easy. The journey continued via Taurdshidakh, and after passing a number of places he came to the frontier at the town of Salty. Two months after his arrival the war was over, and in October he started travelling back.

This must have been the first war in which anaesthesia was used in a great amount. It was also used in the American–Mexican war of 1846–48, but information about this is scarce.[15] In his book: *Rapport medical d'un voyage Caucase*, (St Petersburg, 1849) which was accepted by the censor 14 May 1849, Pirogoff has a long chapter on the use of ether under war conditions, the indications for its use and the experiences he gained. In all, he anaesthetised 100 wounded, of whom only two had rectal ether. The primitive conditions and open fire prevented its use. A number of operations were performed on the battlefield and rectal ether was administrated by one person, who was kneeling between the patient's legs while another, half sitting, held the patient from behind.

Before the book was published, chloroform had been introduced, and Pirogoff was the first to use it in Russia on 30 November 1847 in St Petersburg.[13] Therefore, the book contains a comparison between the use of ether and chloroform. In a long list, divided into all kinds of operations, he has collected information on all the anaesthetics, both ether and chloroform, given in Russia in the period from February 1847 to February 1848. There were a total of 690 anaesthetics, out of which 208 were with chloroform, given within 3 months. Experiences from the war are also described. Chloroform was thought to be superior mainly due to the simplicity of administration and its rapid effect. In those days, speed was a sign of a good surgeon. In this book he tried to evaluate the influence of anaesthesia on the results of the surgery. It is not possible directly to relate the use of anaesthesia on surgical outcome. In a table which included 231 anaesthetics given for low risk operations, there were three deaths, one each for ether, chloroform and rectal ether. Two of these deaths were probably due to anaesthesia.

Pirogoff's conclusion was that anaesthesia probably had no influence on the surgical results. He was probably the first to make some statistical attempt at studying the outcome of surgery under ether anaesthesia.

When he returned to St Petersburg, he worked on a surgical book: *Klinische Chirirgie. Ein Samlung von Monographien*, published in Leipzig in 1854. The Crimean war started in March 1854 and in October of that year Pirogoff was ordered to Sevastopol where he stayed until the war was over in February 1856. During this period, he showed himself to be an excellent organiser of the ambulance service and he introduced an effective triage of the wounded after a careful surgical examination. The wounded were carefully transported and plaster bandages were used; the infected patients were isolated. In cooperation with Grand Duchess Helene Pavlova, he organised a women's corps to nurse the wounded about a year before Florence Nightingale (1820–1910) started her activities in Scutari. Chloroform was mainly used for anaesthesia; Pirogoff wanted to use this for all cases. The Russians performed about 10000 operations during the war.

Pirogoff's experiences from the two wars were published in the book: *Grundzüge der allgemeine Kriegschirurgie. Nach Reminiseenzen aus den Kriegen in Krim und in Kaukasus und aus der Hospital praxis*, (Leipzig 1864).

Due to disagreements with hospital and university administrations, Pirogoff retired from his position at the Academie in 1860 and became curator, first of the University of Odessa, and later of the University of Kiev. He stopped his practical surgical activity in 1866. His new positions required some travelling as he had control of students studying medicine in Germany. Around 1863 he stayed one year in Germany.

During the French–German war, 1870–71, Pirogoff was sent as an observer to French and German hospitals. Here he observed with satisfaction that the principles from his book were in practical use. What he observed was written in another book: *Bericht über die Besichtigung der Militär-Sanitätsanstalten in Deutschland, Lothringen und Elsass im Jahre 1870* (Leipzig 1871). He was an observer in the Russian–Turkish wars in 1877 and 1878, and wrote another book entitled *Army medical service and volunteer aid at the theatre of the war in Bulgaria and in the rear of the armies in the field in 1877–78* (St Petersburg 1879). This book was only printed in Russian.

When Pirogoff was in Kiev, he bought an estate, which he later changed for an estate at Wishnja, 200 km southwest of Kiev. Here he lived when he retired as curator in 1866, and he then developed an interest in farming. He became justice of peace, an office which included taxation of farms and houses, and he was also interested in public and school education.

Pirogoff's 70th birthday was celebrated in Moscow, where he was elected an honorary citizen. Shortly afterwards he became ill with throat symptoms. Professor Theodor Billroth (1829–94) the famous surgeon in Vienna, was consulted, and he claimed the disease was innocent. Some time later, on the 25 November 1881 Pirogoff died from a cancer of the larynx. Later on Billroth declared that he was well aware of the disease, but had abstained from surgery due to the patient's age and physical condition. Billroth had performed the first laryngectomy in 1874.

Pirogoff's place in history

In the history of anaesthesia the name of

Pirogoff is well known, mainly in connexion with the rectal administration of ether, but he ought to have a greater place. He was one of the first to perform systematic experiments with ether, he divided the anaesthetic state into four degrees, which were rather similar to the degrees found by Pierre Jean Marie Flourens (1794–1867) of Paris, in his experiments in February–March 1847.[14] Pirogoff tried ether under war conditions very early on and in more cases than most others. He produced his own equipment for inhalation and rectal administration and he was one of the first to try statistical analysis of the influence of anaesthesia on the operative results. Within surgery his name is well known in connexion with the operation he described, an amputation of the foot without making the leg shorter, and the anatomists knew him for his atlas.

Pirogoff's method of rectal administration of ether was revived in Copenhagen by the surgeon Oskar Wanscher (1846–1906) in 1884[16] and the same year adopted in Lyon by Daniel Mollière (1848–90).[8,14] He had been visited by a Danish surgeon Axel Iversen (1844–92) (in most articles about the subject his name is spelled Yverson), who made him try the method.

It was also in use in the United States at that time. Again, in 1905, the method was tried in Boston by John Henry Cunningham (1877–1969) and Frank Howard Lahey (1880–1953)[4,17] and in England by Dudley Wilmot Buxton (1855–1931) of London, described in his book: *Anaesthetics: their use and administration*, in the 1907 edition.[8,9] Around 1910–14 both W.S. Sutton[9] and John Taylor Gwathmey (1863–1944)[18] modified and used the method. In Denmark the method was again in use in the twenties and thirties[19] and in England rectal oil–ether was used for plastic surgery round 1920.[20] The history of rectal administration of ether has been the subject of two reviews.[8,9]

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CASE REPORT

Acquired C_1 esterase inhibitor deficiency

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Summary

A case of acquired C_1 esterase inhibitor deficiency and its anaesthetic implications is presented. Prophylaxis against angioneurotic oedema using danazol and tranexamic acid is described and the resultant complication of mesenteric venous thrombosis reported.

Key words

Complement; C_1 esterase inhibitor deficiency.
Complications; mesenteric vein thrombosis, angio-oedema.

Osler[1] first described families whose members sustained episodes of angio-oedema which occasionally proved fatal, recurrent transient episodes of abdominal pain due to bowel oedema and transient firm, non-pitting, non-itchy swellings of their extremities. Donaldson *et al.*[2] in 1963 found affected members of this autosomal dominant disorder had serum deficient of an inhibitor of the first component of complement (C_1 esterase inhibitor), which allowed uninhibited complement cascade activation. During complement activation, there is liberation of peptides, particularly plasmin, which increase vascular permeability and thus induce angio-oedema. Deficiency of C_1 esterase inhibitor results in diminished levels of the second and fourth components of complement, but the concentration of the first component of complement remains normal. Caldwell *et al.*[3] in 1972, reported two patients with lymphosarcoma and acquired C_1 esterase inhibitor deficiency. Only one of their patients sustained recurrent attacks of angio-oedema. Since that time, over 30 cases of acquired C_1 esterase inhibitor deficiency have been reported, and most cases have been associated with a B lymphocyte malignancy (lymphoma, lymphosarcoma, chronic lymphatic leukemia, paraprotinaemia or macroglobulinaemia).[4] Unique case reports of the acquired disorder exist in association with myelofibrosis and rectal carcinoma. When associated with B cell malignancies, antibodies have been detected that are directed against the abnormal immunoglobulins present on the malignant B cells,[5] so-called anti-idiotypic antibodies. Reactions between the immunoglobulins and the anti-idiotypic antibodies cause activation of the first component of complement and then secondary reduction in C_2, C_4 and C_1 esterase inhibitor concentrations. The low C_1 concentration, late age onset of angio-oedema and absent family history serve to distinguish between the acquired

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and hereditary conditions and obviously serve as a marker of underlying malignancy.

In both the acquired and hereditary conditions, life threatening angio-oedema may occur after oropharyngeal surgery, tracheal intubation and even stress, though in many instances angio-oedema occurs without any obvious precipitating factor. Adrenaline, corticosteroids and antihistamines are of no proven benefit as prophylactic agents and do not abort attacks of angio-oedema once they have started. Danazol is of definite prophylactic value in both the hereditary and acquired disorders as it probably increases hepatic synthesis of C_1 esterase inhibitor.[4]

Tranexamic acid is advocated as both a general[6] and peri-operative prophylactic agent[7] and it acts as both a direct inhibitor of C_1 activation as well as an inhibitor of plasmin activation. It also has antifibrinolytic activity and thus increases thrombotic tendency.

The purpose of this report is to describe a case of acquired C_1 esterase inhibitor deficiency, to indicate the potential anaesthetic problems that may be encountered in the management of such a case and to report a serious complication of tranexamic acid prophylaxis.

Case history

The patient, a 54-year-old female, attended Casualty with severe upper airways obstruction secondary to gross unilateral oedema of her tongue. She had experienced four similar episodes but with no respiratory difficulties in the previous 18 months. All attacks occurred at night, with no apparent precipitating factors and there was no family history of angio-oedema. The casualty officer administered hydrocortisone, chlorpheniramine and intramuscular adrenaline and she was transferred to the intensive therapy unit on a 21:79 mixture of oxygen and helium. Her condition gradually improved over the next 4 days.

On investigation she was found to have low levels of C_1 esterase inhibitor protein, C_4 and C_1q, i.e. acquired C_1 esterase inhibitor deficiency. She was commenced on danazol 200 mg tds for prophylaxis and investigated for the usually associated underlying malignancy. Despite a thrombocytosis ($688\,000 \times 10^9$/litre), the bone marrow examination was inconclusive, and a left ovarian mass demonstrated on pelvic CT scan became the likeliest site of malignancy.

In view of her episodes of angio-oedema, pelvic clearance was performed under epidural anaesthesia using bupivacaine 0.5% plain. Danazol was continued pre-operatively and, in addition, she received tranexamic acid 1 gm with the premedication, and 6-hourly for 5 days postoperatively. The operation was uneventful and she received an epidural infusion of bupivacaine 0.25% for postoperative analgesia for 36 hours. Histology of the mass was that of benign cystic teratoma.

On the eighth postoperative day, the patient developed epigastric pain and vomiting. Tranexamic acid 1 gm was given intravenously on the assumption that this was bowel mucosal oedema. The pain worsened and a clinical diagnosis of mesenteric vascular occlusion was made. Despite anticoagulation and maintenance of fluid balance, her condition deteriorated and she was referred for laparotomy.

After a rapid sequence induction of anaesthesia using methohexitone, suxamethonium and tracheal intubation with an oral, cuffed polyvinyl chloride tracheal tube, anaesthesia was maintained with halothane, papaveretum and tubocurarine. The venous plexus of most of the small bowel mesentery was thrombosed, so an iatrogenic omphalocoele was fashioned to allow better demarcation of the necrotic bowel, and the patient's lungs were ventilated for 7 hours on the intensive therapy unit. At re-exploration, all the small bowel except 18 inches of viable jejunum was excised. Ventilation was continued for 3 days and her trachea was then extubated uneventfully. Five days later she was again anaesthetised for repair of a perforated patch of gangrenous bowel and had no postoperative problems. She has made a good recovery and long term prophylaxis against angio-oedema will be reviewed when her intestinal function is stable.

Discussion

Acquired C_1 esterase inhibitor deficiency is a rare condition, so its treatment has not been subjected to controlled study. The only therapeutic measures reported in the literature are treatment of the underlying malignancy and long term prophylaxis using danazol.[4] Further extrapolation from the treatment of the hereditary disorder may not necessarily be valid.

Danazol is a derivative of ethyinyl-testosterone with minimal androgenic effect. The mechanism

Table 1. Immunological response to danazol prophylaxis

	Pre-treatment	Post-treatment
C_1 esterase inhibitor (g/litre) (normal range 0.18–0.26)	0.12	0.41
C_4 (g/litre) (normal range 0.2–0.49)	<0.1	<0.1

by which it increases C_1 esterase inhibitor activity is unknown, although increased hepatic production of C_1 esterase inhibitor appears most likely. The effect is rapid, with C_1 esterase inhibitor levels increasing to near normal levels within 5 days and decreasing to near pre-treatment levels 12 days after stopping treatment.[8] This is not necessarily accompanied by C_1q and C_4 levels returning to normal,[9] as our patient also demonstrated (Table 1).

As plasmin is known to activate C_1, and as this pathway may be especially responsible for initiating angio-oedema secondary to trauma, the use of an inhibitor of plasminogen activation such as tranexamic acid has been recommended in short peri-operative courses for dental and surgical procedures in the hereditary form of angio-oedema. The C_4 levels in our patient remained low on danazol, which suggested continued accelerated C_1 activation despite high C_1 esterase inhibitor levels, so tranexamic acid was added to the peri-operative prophylaxis to inhibit plasmin as a source of this continued C_1 activation.

The danger of thrombosis when using an antifibrinolytic agent, especially in patients with possible haematological malignancy, was demonstrated in our case. We therefore do not recommend the routine use of tranexamic acid for perioperative prophylaxis in these patients. Danazol appears safe and effective, despite continuing abnormalities in the complement pathway, and it may have prevented angio-oedema during the two subsequent general anaesthetics.

Acute attacks are unresponsive to steroids, antihistamines and adrenaline, so transfusion with fresh frozen plasma, C_1 esterase inhibitor concentrate or plasmaphoresis would appear to be reasonable but untried options in the acquired condition.

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CASE REPORT

Atypical plasma cholinesterase

Case clustering

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Summary

The plasma cholinesterase status of 22 people resident in the same small town was investigated. A high incidence of the atypical cholinesterase gene was found.

Key words

Enzymes; plasma cholinesterase.
Neuromuscular relaxants; suxamethonium.

Serum or plasma cholinesterase (pseudocholinesterase) is an enzyme found in the plasma and in most tissues of the human body. It has a lipoprotein structure and appears to be chiefly concerned with ester hydrolysis. Its physiological importance, however, is unresolved, since a congenital absence has no apparent ill effects.[1] The enzyme is of interest mainly because of its role in metabolising the depolarising muscle relaxant drug suxamethonium (scoline); most of a normal dose is removed in the first minute following intravenous administration. Introduced into anaesthetic practice in the 1950s, suxamethonium remains a popular drug; its quick onset and rapid recovery are especially useful. Despite anecdotal reports of prolonged paralysis following its use—scoline apnoea—it was several years before it became clear that several types of plasma cholinesterase exist[2] and that the 'defective' enzymes showed a reduced or absent ability to metabolise the drug. The enzyme variants are transmitted as Mendelian autosomal recessives and are identified by the degree to which their activity is inhibited by the addition of various chemical reagents. Five variants have been clearly identified so far (Table 1).

If a sensitive individual is identified, screening is offered to all appropriate relatives and warning cards issued to those found to be homozygous for an abnormal enzyme. The position of heterozygotes is less clear, since the majority will suffer no clinically significant prolongation of neuromuscular blockade. However, a wide variety of conditions, including pregnancy, can reduce cholinesterase activity, resulting in an acquired sensitivity.[3] British practice is to issue warning cards only to female heterozygotes who may become pregnant, since suxamethonium is routinely used in obstetric anaesthetic practice.

Case history

A 76-year-old man was admitted for an open prostatectomy. He was otherwise healthy and

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Table 1. Type, designation and frequency of homozygous plasma cholinesterase variants

Enzyme type	Designation	Frequency (%)
Usual	($E_1^uE_1^u$)	96
Atypical	($E_1^aE_1^a$)	0.05
Fluoride resistant	($E_1^fE_1^f$)	0.00067
Silent	($E_1^sE_1^s$)	0.001
C5 variant*	Enhanced activity	10

*Not allelic with other cholinesterase variants.

Table 2. Genotyping and plasma cholinesterase activity of family 1

Relation	Cholinesterase activity (normal 3.0–9.6 kU/litre)	Genotype
Patient	0.9	Homozygote
Brother (twin)	1.3	Homozygote*
Sister	1.4	Homozygote†
Brother	5.8	Normal
Sister	4.8	Heterozygote
Sister	3.7	Heterozygote
Sister	3.5	Heterozygote
Daughter	4.3	Heteroxygote
Daughter	2.0	Heterozygote
Grand-daughter	3.5	Heterozygote
Nephew	4.5	Heterozygote
Nephew	1.9	Heterozygote

*Previous surgery: bilateral total hip replacement.
†Previous surgery: three stage bowel resection.

had previously undergone several surgical operations. These included tonsillectomy, appendicectomy, cholecystectomy (plus three further explorations to deal with complications), total hip replacement and a variety of minor procedures. He specifically denied any previous anaesthetic problems. A spinal anaesthetic was administered, but the analgesia produced proved inadequate and general anaesthesia was induced. Suxamethonium 75 mg was administered and tracheal intubation carried out. Following this, all efforts to re-establish spontaneous ventilation failed and the patient was mechanically ventilated until the conclusion of the operation 2 hours later. Efforts to restore spontaneous ventilation were again unsuccessful and no cause could be found for the apnoea. The patient's cardiovascular system had remained stable, and cephalic spread of the spinal anaesthetic to involve the cervical spinal cord was considered unlikely. There were no pupillary changes to indicate a neurological cause and there was no response to the respiratory stimulant doxapram. Mechanical ventilation was continued and blood sent for plasma cholinesterase levels, although it was considered unlikely that a suxamethonium sensitivity could have escaped previous detection. However, the cholinesterase activity was reported as 0.9 kU/litre (normal 3.0–9.3) and a presumptive diagnosis of suxamethonium sensitivity was made. Suxamethonium undergoes slow hepatic metabolism and the patient was receiving fresh whole blood (in which plasma cholinesterase is stable) to replace intra-operative losses, so treatment was expectant. Four hours after suxamethonium administration, the patient began to regain muscle tone and one hour later he was weaned from the ventilator; subsequently he made an uneventful recovery.

A decision was made to screen members of the patient's family who lived locally. Blood samples were obtained from 11 relatives, the plasma cholinesterase activity measured and genotyping carried out (Table 2).

These results are of considerable interest, since there are a number of unusual features about this family. The first is that three homozygotes could undergo a wide variety of surgery and survive into their late 70s without being exposed to suxamethonium, although an Australian patient was

Table 3. Genotyping and plasma cholinesterase activity of family 2

Relation	Cholinesterase activity (normal 3.0–9.6 kU/litre)	Genotype
Halfbrother	5.2	Normal
Sister	3.0	Heterozygote
Sister	3.2	Heterozygote
Mother	3.2	Heterozygote
Aunt	4.2	Heterozygote
Niece	3.4	Heterozygote
Niece	3.4	Heterozygote
Nephew	4.2	Heteroxygote
Nephew	3.8	Heterozygote
Nephew	3.4	Heterozygote*

*Heterozygote for atypical and fluoride resistant genes ($E_1^aE_1^f$)

diagnosed following prolonged apnoea at the age of 91.[4] The second interesting feature was to find identical twins with this condition. Although in theory this should occur with a frequency of 1:800 000, it does not appear to have been previously documented. The next unusual aspect followed the admission of a second patient who, like the first, was a native of Dromore, County Down, Northern Ireland. Previously diagnosed as being homozygous for atypical cholinesterase, he denied being related to the first patient in any way. Screening was then offered to the family of the second patient (Table 3); the majority of these, like the first family, were resident in Dromore.

Discussion

Although this area is not traditionally regarded as one in which significant inbreeding occurred (R.S.J. Clarke, personal communication), census returns show that until the turn of the century approximately 90% of the population was born in or near the town.[5] The high incidence of this rare gene in such a small population (presently 3140) must therefore give rise to speculation of a gene pool for the characteristic in this area. Eighteen of the 22 people screened live in the town, but most families declined further screening when they discovered that they were heterozygote and unlikely to be severely affected. In total, only about 20% of those possibly affected cooperated in screening and it is probable that large numbers of heterozygotes remain undetected. Consequently, the town will continue to produce greater than expected numbers of patients with scoline apnoea.

Acknowledgment

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Anaesthesia, 1986, Volume 41, pages 844–846

CASE REPORT

Prolonged neuromuscular blockade following suxamethonium in a patient with a normal genotype

D. J. SAPSFORD AND G. H. BUSH

Summary

A patient is described who developed prolonged apnoea following a single normal dose of suxamethonium which was shown by nerve stimulation to be due to persistent neuromuscular blockade. The plasma cholinesterase profile demonstrated a normal genotype.

Key words

Neuromuscular relaxants; suxamethonium.
Enzymes; cholinesterase.

Sensitivity to suxamethonium which produces prolonged apnoea is usually due to an abnormal plasma cholinesterase activity, the dibucaine number and/or fluoride number, demonstrating an abnormal genotype. Patients with prolonged apnoea after suxamethonium in whom a normal genotype can be shown usually have factors causing central nervous system depression, such as inhalational agents or hypocapnia. The aetiology of the apnoea in these situations cannot be precisely defined in the absence of neuromuscular transmission monitoring. In one series[1] of 225 patients referred to the Danish Cholinesterase Research Unit because of prolonged apnoea following suxamethonium, 63 patients (28.1%) showed a normal cholinesterase genotype. A careful review of the anaesthetic records, and re-exposure to suxamethonium, left 22 patients (10.7%) without explanation for their apnoea. It is the conclusion of that report that probably 10% of patients with prolonged apnoea after suxamethonium have hitherto unknown genotypes. To date, no case of an abnormal reaction to suxamethonium in a patient with a reported normal genotype has been reported where this has been confirmed using a nerve stimulator.

Here we describe a patient with prolonged apnoea following suxamethonium, who had a normal genotype and in whom neuromuscular transmission was monitored.

Case history

A 12-year-old girl weighing 51 kg was admitted for an elective examination under anaesthesia and sigmoidoscopy. She had a history of rectal bleeding for 4–5 weeks and occasional abdominal pain. There were no other symptoms; she was not receiving any medication, had no past medical history to note and had never had a general anaesthetic. It was reported that she was allergic to elastoplast. On examination, apart from being slightly overweight, she was a healthy, normal girl.

She was premedicated with oral trimeprazine

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30 mg at 7 am and given intramuscular morphine sulphate 10 mg and atropine 600 μg at 10 am. Anaesthesia was induced with thiopentone 200 mg and neuromuscular blockade was produced with suxamethonium 75 mg at 11.52 am; the trachea was intubated with a 7.0 mm uncuffed Portex orotracheal tube. Anaesthesia was maintained with nitrous oxide and oxygen in a 70%:30% mixture with manual intermittent positive pressure ventilation. The procedure was performed and spontaneous recovery from the suxamethonium neuromuscular blockade was awaited.

This did not occur, so 5% carbon dioxide was added to the fresh gas mixture and ventilation continued. Twenty minutes after induction there was no spontaneous respiratory activity and muscle tone was absent. Peripheral nerve stimulation (Bard Biomedical PNS4500) and capnography (Datex Normocap) were instituted. End tidal carbon dioxide was maintained at 5.3–6.7 kPa. There was no detectable twitch or response to a 50 Hz tetany to stimulation of greater than 40 milliamps to both ulnar and tibial nerves; the electrodes were therefore left in place over the night ulnar nerve. At 105 minutes the first twitch of the train-of-four was felt (no transducer or EMG was in use) and at 132 minutes there were four twitch responses to the train-of-four with obvious fade. At 143 minutes there was no detectable fade on train-of-four stimulation and spontaneous movement and respiration soon returned. Within the next 5 minutes, respiration was judged to be adequate and the child's trachea was extubated. When she was able to make sustained limb movements and head lift, she was returned to the ward.

Three days later, venous blood was taken from the whole family and sent to the biochemistry laboratory. In view of the normality of these results (Table 1), a further specimen of the patients venous blood was sent to the cholinesterase unit at the Royal Postgraduate Medical School, which confirmed the previous findings.

Discussion

The development of prolonged neuromuscular blockade (143 minutes) following suxamethonium in this patient of normal genotype was demonstrated by repeated nerve stimulation. On return of neuromuscular transmission the block was of a non-depolarising type, characterised by tetanic fade and fade in the train-of-four, the so called phase II block.[2] The development of a phase II block is determined by continuous or repeated exposure of the end plate to suxamethonium. This, in turn, depends on the amount injected, the speed of injection, esterase activity, body temperature and blood flow through the muscle. It usually develops after a dose of 3–5 mg/kg,[3] but tetanic fade and post-tetanic facilitation have been reported with smaller doses in adults.[4,5]

However, in our patient there was complete neuromuscular blockade for 105 minutes and slow recovery up to 143 minutes, as shown by gradual return of the train-of-four. The cause of apnoea could not have been due to hypocapnia, or central nervous system depression due to inhalational agents or morphine. This points to diminished cholinesterase activity as being the cause, but this could not be confirmed by laboratory measurements.

Suxamethonium is usually hydrolysed in plasma in a few minutes by acetylcholine-acetylhydrolase (EC 3.1.1.8) known as plasma cholinesterase. If the activity of this enzyme is abnormal, the patient given a normal intubating dose of suxamethonium may have respiratory

Table 1.

	Cholinesterase activity	Dibucaine number	Fluoride number	Genotype	
Normal	80–120 units	>80	>55	E_1^u	E_1^u
Alder Hey results					
Patient	111 units	83	57	E_1^u	E_1^u
Father	149 units	82	68	E_1^u	E_1^u
Mother	108 units	83	61	E_1^u	E_1^u
Royal Postgraduate Medical School results					
Patient	108 units	81	58	E_1^u	E_1^u

insufficiency for several hours. Sixty five percent of all cases of prolonged neuromuscular blockade following the administration of suxamethonium are due to genetic factors;[6] these are expressed as four allelic recessive genes at locus E_1 (usual E_1^U atypical E_1^a, fluoride resistant E_1^f, and silent E_1^s). Cholinesterase activity can be measured in several ways. Usually, the cholinesterase acts upon a substrate and the products of hydrolysis are measured per unit time. Hydrogen ion liberation allows the pH to be used as an indicator. More recently, spectrophotometric methods have been used.[7] Benzoylcholine is the usual substrate used and together with inhibitors (dibucaine and sodium fluoride) will determine the genotype, but it does not give any unambiguous relationship between measured enzyme activity and the reaction to suxamethonium.[8,9] Only if the genotype is known is it possible to predict the action of suxamethonium.

The use of other substrates may offer better correlation between measured enzyme activity and reaction to suxamethonium. Proprionylthiocholine and suxamethonium have been suggested as alternative substrates,[9,10] but the accuracy of the method remains to be proven: this method is therefore only rarely employed.

A recent paper[11] describes the use of suxamethonium as a substrate for the estimation of cholinesterase activity using the recommended proprionylthiocholine method. This assay offers a more effective method of screening for sensitive individuals and is more reproducible than previous attempts using this substrate. An abnormal cholinesterase activity with this determination demonstrates the E_1^{su} genotype. Our laboratory is investigating the possibility of using this method and we hope to analyse this patient's serum. It would be interesting to speculate whether this new technique, using suxamethonium as the substrate, will identify a new genotype.

Acknowledgments

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Anaesthesia, 1986, Volume 41, pages 847–849

CASE REPORT

Accidental subdural catheterisation

A. LEE AND K. W. DODD

Summary

A case of accidental subdural catheterisation is presented, and its course is compared with previously reported subdural injections of local anaesthetic agents. The importance of obtaining proof of the site of malposition of an epidural catheter is stressed.

Key words

Anaesthetic techniques, regional; epidural, subdural.
Complications; hypotension.

A case of subdural catheterisation during attempted epidural placement was confirmed radiographically and reported for the first time in 1975.[1] Only three other documented cases which have been confirmed have been reported.[2-4] Several reports of presumed subdural injections of local anaesthetic agents have been published and these have been based on the time course, extent of spread and complications believed to be associated with subdural injection.[5-9] Much of this is conjectural, as there are so few proven subdural catheterisations. The case presented here differs from what has previously been expected following subdural administration of local anaesthetic.

Case history

A 30-year-old nurse was admitted in established labour. She was 1.52 m in height, weighed 82 kg and had previously undergone Caesarean section for failure to progress. On this occasion, the baby's head was high but pelvimetry was acceptable and it was intended that she should have a trial of labour with early recourse to Caesarean section should this prove necessary. Her last anaesthetic, which had been for her Caesarean section, had been complicated by bronchospasm and hypotension. There was no evidence of aspiration occurring at the time and it was suggested in the notes that the most likely cause was thiopentone or suxamethonium hypersensitivity. No investigations had been performed to confirm or refute this. In view of this history it was thought prudent to establish epidural analgesia at an early stage.

The epidural space was identified using a 16-gauge Tuohy needle and loss of resistance to saline at L_{2-3}. This was uneventful and the ligamentum flavum was easily felt; there was no suggestion of dural or venous puncture with the needle. A triple end hole epidural catheter was passed through the needle without difficulty and the needle eased backwards over the catheter

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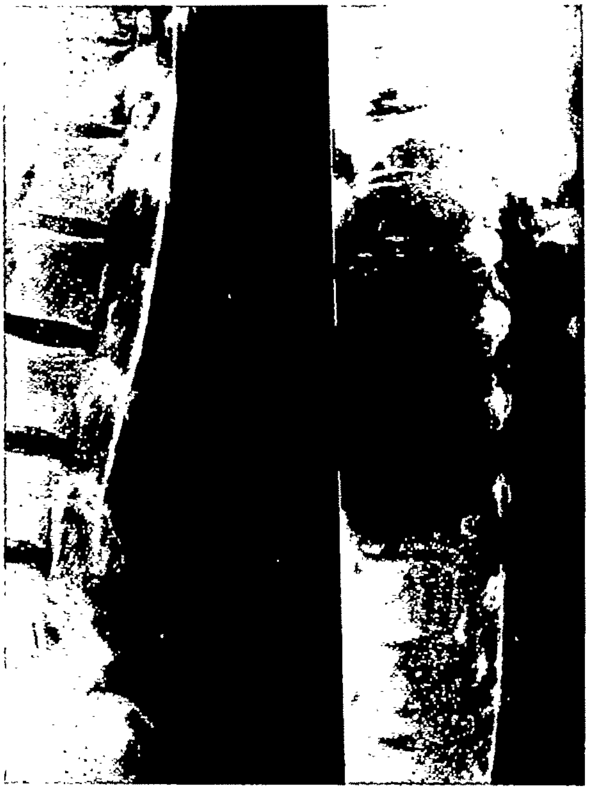

Fig. 1. Lateral view of thoracolumbar spine showing contrast medium spreading from the fourth lumbar to the sixth thoracic vertebra.

leaving 3 cm in the space. There was no drip back of fluid or blood through the catheter and aspiration was negative. A 0.22 μm filter was attached and 6 ml of 1% lignocaine plain solution injected as a test dose. Seven minutes after administration of the test dose the patient had no symptoms suggestive of either vascular or subarachnoid injection and 10 ml of 0.25% bupivacaine plain solution was therefore injected through the catheter. No fluid preload was given, but a freely running infusion of Hartmann's solution was established prior to siting the epidural.

Fifteen minutes after injection of the bupivacaine the patient had good pain relief. Ten minutes later, while in the left lateral position, she became hypotensive and her blood pressure decreased from 130/100 mmHg to 90/50 mmHg. Hartmann's solution 1000 ml was administered and her blood pressure rapidly increased to 130 mmHg systolic. At this time analgesia to pinprick extended to T_4 on the right side and C_8 on the left side. Breathing and speech were normal and corneal reflexes were present. One hour and 5 minutes after injection of the bupivacaine the block receded, contraction pains returned and sensation to pinprick became normal in all dermatomes. A further 7 ml of 0.25% plain bupivacaine was then injected. Again the time course of onset resembled that of an epidural injection, but the block extended from T_3–L_4 on the right side and T_9–L_4 on the left side after 20 minutes. The patient also developed a right Horner's syndrome and 15 minutes later she complained of a stuffy right nostril. Corneal reflexes were retained. No other features developed and the block again regressed in one hour and 40 minutes. The catheter was left *in situ* for subsequent radiographic confirmation of its position and the patient underwent uneventful Caesarean section using a second catheter sited at the L_{3-4} interspace.

The next day 10 ml of iopamidol 200, a water soluble radiographic contrast medium, was injected through the original catheter and a lateral radiograph of the dorsal spine was taken. This clearly demonstrated the catheter to be in the subdural space (Fig. 1).

Discussion

Subdural placement of an epidural catheter has been confirmed on four occasions.[1-4] In three of these cases the onset time to maximal block and the time to complete regression of the block were accurately determined.[1-3] The time to maximal onset ranged from 20–30 minutes with 0.5% bupivacaine solution and was 21 minutes with 2% chloroprocaine. The time to complete regression ranged from 135–150 minutes with 0.5% bupivacaine and was 53 minutes with 2% chloroprocaine. The present case corresponds to these reports; the onset time was at the upper end of the normal range for epidurals, and the time to complete regression was well within the expected time limits.[10-12] In all cases, motor blockade was minimal or absent, hypotension was easily treated or absent and the block extended cranially rather than caudally. Two of the reported cases were predominantly unilateral and trigeminal involvement was reported in one case. In the present case a Horner's syndrome was present.

These findings are in marked contrast to some of the cases which have been reported without radiographic confirmation and attributed to subdural block. Confirmed cases do not support the suggestion that subdural blockade is characteristically very slow in onset, slow in regression and associated with intracranial spread causing apnoea, coma and total paralysis.[5-7] In other cases ascribed to subdural block, dural penetration occurred in four and marked difficulty was experienced in placement of the epidural catheter in one.[7,13-17]

In a series of 100 patients undergoing total spinal anaesthesia, the onset time to maximal block ranged up to 45 minutes and 11% had no significant hypotension.[18] Consequently, subarachnoid spread of local anaesthetic agent cannot be excluded merely because onset time is prolonged. The ascent of radiographic contrast medium in the subdural space is very rapid and a long onset time following local anaesthetic injection would be surprising.

The unusual events reported following some epidural injections of local anaesthetic agents cannot always easily be explained using the small amount of information at present available. It is essential that in all cases where bizarre features follow local anaesthetic injection, the epidural catheter is retained for subsequent radiographic confirmation of its position.

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Anaesthesia, 1986, Volume 41, pages 850–852

CASE REPORT

Intercostal neuralgia following stellate ganglion block

An infrequent complication

M. I. D. McCALLUM AND C.J. GLYNN

Summary

The case is described of a 78-year-old female patient who experienced temporary but severe chest wall pain following stellate ganglion block. The possible mechanisms and treatment of this complication are discussed.

Key words

Anaesthetic techniques, regional; stellate, sympathetic block.
Complications; chest pain.

Case history

A 78-year-old patient attended Abingdon Pain Relief Unit Outpatient Department with a 9-month history of burning pain and hyperaesthesia in the ulnar border of her right hand following a Colles' fracture of the limb. Her general health was otherwise excellent and she remained very active for her age.

A post-traumatic sympathetic dystrophy had been diagnosed earlier and initially treated with amitriptyline and sodium valproate. Drug therapy had proved ineffective and was discontinued following her complaints of impaired mental function. An intravenous sympathectomy had then been carried out, using guanethidine and this resulted in significant pain relief.[1]

Following a favourable response, one week earlier, to peripheral (i.e. postganglionic) sympathetic blockade of the limb, it was decided at her next outpatient attendance to produce a more central (i.e. ganglionic) sympathetic blockade, by a local anaesthetic block of the stellate ganglion.

A stellate ganglion block was performed according to the method described by Moore,[2] using 10 ml of plain bupivacaine 0.5% solution. Signs of sympathetic blockade were soon evident, with appearance of ipsilateral ptosis, miosis, conjunctival injection and vasodilatation of the right hand. In addition, hoarseness of the voice suggested spread of the local anaesthetic solution to involve the recurrent laryngeal nerve

Following reassurance regarding the voice changes, the patient appeared pleased with the result, and described the hand as warm and pain free. After a further hour, during which no adverse effects were observed, the patient was allowed to leave the outpatient department with her escort. Subsequent events were only recounted at a return appointment 2 weeks later, since immediate care was managed by her general practitioner who did not contact hospital staff.

Two hours following the stellate block, she experienced sudden onset of severe right-sided chest pain extending downward from the axilla to the level of the tenth rib. The pain was constant, stabbing in character and caused considerable

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distress. There was no dyspnoea to suggest the possibility of a pneumothorax.

Clinical examination and electrocardiography performed by the general practitioner failed to reveal any cause for the pain. Intramuscular pethidine had no influence on the intensity of the pain and relief was only obtained when it spontaneously subsided and disappeared approximately 2 hours after its onset. No further adverse effects were experienced and it was noted that the treated limb had remained pain free during the episode.

In view of the above complication following stellate ganglion block, her subsequent management consisted of intravenous sympathectomies repeated on several occasions and this enabled her to be discharged from the clinic 6 months later with almost complete remission of her pain.

Discussion

Stellate ganglion block using local anaesthetic solutions has a recognised incidence of complications; the commonest of these are recurrent laryngeal or phrenic nerve block, vertebral artery puncture, pneumothorax and intrathecal injection.[3] Intercostal neuralgia has been described as a common complication following stellate ganglion block,[4] although the paucity of the published literature does not confirm this. However, when such pain does occur, it is obviously distressing and may lead to erroneous diagnosis and therapy.

The delayed onset of chest wall pain which we describe does not lend itself to the simple explanation of trauma to adjacent structures, nor does it explain the very circumscribed duration or anatomical distribution. However, pain syndromes following surgical sympathectomy are well documented[5] and have been associated with an abnormal increase in sympathetic efferent activity.[6] The time lag between the application of a stimulus and its subsequent sensation has been emphasised as a characteristic of stimulation of sympathetic rather than somatic nerves.[7]

The sympathetic nervous system is efferent, and therefore would not be expected to transmit sensory activity directly, but there is evidence to show that a hyperactive sympathetic nervous system may elicit pain.[8]

Walker and Nulson elicited reproducible patterns of pain response (in five out of 12 patients) by direct electrical stimulation of the second and third thoracic ganglia of patients who had undergone surgical cervical sympathectomy.[8] Two patients experienced localised pain in the back and chest. They concluded that in patients with causalgia, there appeared to be a relationship between peripheral effects of sympathetic activity and the production of pain.

Tracy and Crockett have shown increased sympathetic nervous activity in patients with postsympathectomy pain by demonstrating increased sweating in the anterior thigh, which was absent in patients who did not develop pain following surgical lumbar sympathectomy.[6] It has been suggested by Raskin that the pain of this syndrome, which is both temporally and topographically related to the recovery of sympathetic innervation, may indicate increased activity of the sympathetic nervous system as a causal factor.[5]

Chest wall pain following stellate ganglion block is an unusual but distinct complication. This case may represent an example of pain arising from abnormal sympathetic nervous activity, which occurred as the neural blockade associated with bupivacaine waned. The observation that the treated limb remained pain free, raises the interesting speculation as to what extent the previous postganglionic sympathetic block with guanethidine (half life 5 days) gave protection from a pain process which had arisen centrally.

It has been stressed by Moore[2] that any successful block of the stellate ganglion normally involves block of several adjacent sympathetic ganglia above and below, therefore causing an extensive disturbance of sympathetic function. In keeping with other postsympathectomy pain syndromes, the pre-existence of abnormal sympathetic hyperactivity may have made this complication more likely in the patient described.

If the condition is unrecognised and an inaccurate diagnosis made, inappropriate and possibly dangerous treatment may be prescribed. Conventional supportive therapy for postsympathectomy pain with analgesics, e.g. salicylates and codeine, usually proves to be inadequate.[5] However, if the condition is recognised, transcutaneous electrical nerve stimulation, which is of proven effectiveness in treating pain following lumbar sympathectomy, may be beneficial. Favourable responses to anticonvulsant drugs, e.g. carbamazepine and phenytoin, have been claimed during the treatment of surgical postsympathectomy pains[5] and this may represent an interesting new approach.

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CASE REPORT

Epidural anaesthesia in von Hippel-Lindau disease

Management of childbirth and anaesthesia for Caesarean section

A. J. MATTHEWS AND J. HALSHAW

Summary

The management of childbirth, including epidural anaesthesia for Caesarean section is described in a patient with von Hippel-Lindau disease. The reasons for the choice of epidural anaesthesia are explained and the anaesthetic significance of the disease is discussed.

Key words

Anaesthetic techniques, regional; epidural.
Complications; von Hippel-Lindau disease.

Von Hippel-Lindau disease is a familial disorder and has an autosomal dominant pattern of inheritance. It is classified as a phakomatosis and is characterised by angiomatous hamartomas of the retina, central nervous system (CNS) and viscera.[1] Of more than 25 distinct clinical manifestations, six commonly produce significant morbidity: retinal, cerebellar, medulla oblongata and spinal haemangioblastomata, renal cell carcinoma and phaeochromocytoma. Cerebellar haemangioblastoma and renal cell carcinoma are the most frequent causes of death.[4]

The retinal lesions, known as angiomatosis retinae, were described by von Hippel in 1904. Lindau later described the syndrome including retinal and cerebellar neoplasms and noted the frequent occurrence in families.[3] The reported incidence of angiomatosis retinae is one in 22 500 patients seen by ophthalmologists and CNS haemangioblastomata occur in about 20% of cases.[1] Cerebellar haemangioblastomata account for 2% of brain tumours; they are the fourth most common tumour of the posterior cranial fossa and are associated with von Hippel-Lindau disease in 5–20% of cases.[4]

If left untreated, the retinal lesions can lead to glaucoma and blindness. Treatment with laser photocoagulation, however, can halt such progress.[5] Once the cerebellar tumour becomes symptomatic, the course is one of progressive neurological impairment leading to death over days, months or years if untreated. Successful treatment of one lesion, however, often permits expression of other manifestations and there is also a high rate of recurrence of the original, incompletely resected tumour. There is no age at which the patient is no longer at risk.[6]

Case history

A fit 21-year-old housewife, pregnant for the first time, was admitted to the antenatal ward at 39 weeks gestation. She was known to have inherited von Hippel-Lindau disease from her father, who had died at the age of 48 years following treatment for a cerebellar haemangioblastoma.

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In the past the patient had had a craniotomy aged 18 years, at which a cerebellar haemangioblastoma was excised and she had been left with a ventriculoperitoneal shunt *in situ*. She had also had regular treatment with photocoagulation for angiomatosis retinae.

Because of the potential presence of an undetected CNS haemangioblastoma, and the rise in arterial pressure associated with contractions, a spontaneous vaginal delivery was felt to be contraindicated. Similarly, a general anaesthetic requiring a rapid controlled intubation sequence was felt to present a theoretical risk in the hypertensive response to intubation. A subarachnoid needle could theoretically perforate a spinal cord haemangioblastoma, causing a haematoma and so an epidural technique was employed.

Following a circulatory preload with 1000 ml of Hartmann's solution, 20 ml of 0.5% bupivacaine with one in 200000 adrenaline was injected via an epidural catheter inserted into the L_{2-3} interspace in the sitting position. A further 4 ml of this solution in the supine position with left lateral tilt completed the block up to segmental level T_5. Satisfactory analgesia resulted for lower segment Caesarean section and arterial pressure, monitored by oscillotonometer, remained steady around 100/60 mmHg throughout the procedure, falling only to 90/60 mmHg during a sudden loss of about 800 ml of blood from the placenta during delivery of the head. A further 1000 ml of Hartmann's solution was administered during the course of the operation and syntocinon 10 i.u. was given following delivery of the anterior shoulder, with no notable change in arterial pressure.

Postoperatively, the patient was observed for symptoms and signs of raised intracranial pressure for 24 hours. She made a complete and uneventful recovery.

Discussion

A computer search of the literature revealed no previous case reports in the anaesthetic literature, although von Hippel-Lindau disease is mentioned in anaesthetic texts on rare and familial diseases.[7,8] These note the association with phaeochromocytoma, polycystic kidneys and polycythaemia, and the fact that the neurosurgical operations can be prolonged.

The retinal and CNS tumours are similar histologically, consisting of complete vascular units comprising arteriole, capillary bed and venule. The capillaries leak plasma and blood because they lack endothelial tight junctions. Thus, the retinal tumours are associated with retinal exudates[1] and in 80% of cases the cerebellar tumours are found lying as a nodule in the wall of a cyst. The cerebellar tumours usually cause symptoms and signs related to their gradually enlarging size, namely headache, vomiting, ataxia and papilloedema.[4] Rarely, however, they present as a subarachnoid haemorrhage.[9] Since there is a 10% risk of recurrence of the cerebellar tumour,[4] there was a definite, if slight, increased risk of a subarachnoid haemorrhage in our patient.

Normal labour results in a rise in arterial pressure of 30 mmHg during contractions in the second stage. Cerebrospinal fluid (CSF) pressure has also been found to rise by as much as 7.0 kPa during contractions in the second stage.[10] Both rises are less marked during adequate analgesia. Since the pressure rises are in phase (the CSF pressure rise in pain free labour is attributed to a rise in arterial and venous pressure), there is probably not a great increase in intracranial arterial transmural pressure during contractions; the risk of haemorrhage from an intracranial haematoma is therefore probably low. During expulsive efforts, however, pressure rises are even higher and overall it seems good policy to avoid the risk of subarachnoid haemorrhage by avoiding normal labour in these patients.

Ergometrine also causes a considerable rise in arterial pressure which is potentiated by vasopressors. This is thought to give rise to a risk of cerebrovascular accident even in patients who are not at risk and even if given several hours after the vasopressor.[10] In our patient, syntocinon was not associated with any detectable change in arterial pressure.

Spinal cord haemangioblastomata occur in less than 5% of cases of von Hippel-Lindau disease and often go unnoticed clinically.[6] They may present with spontaneous subarachnoid haemorrhage or give rise to progressive neurological symptoms over a variable time span from one month to 10 years. They may be found at any level in the spinal cord, but most often in the cervicothoracic or thoracolumbar regions.[11] They are usually intramedullary in the posterior columns, close to the pia mater.[12] Thus, the risk of accidental puncture with a subarachnoid needle below the L_{1-2} interspace should be low.

Computer tomography has been recommended as the initial investigation of choice for intracranial and spinal tumours and renal mass in these patients.[2] In our case, scanning was not easily available and it was felt that it would make no difference to the anaesthetic, since even tumours too small to be detected could have caused a subarachnoid haemorrhage.

In conclusion, in the absence of contra-indications, elective Caesarean section under epidural anaesthesia appears to be a sensible choice for management of childbirth in patients with von Hippel-Lindau disease.

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CASE REPORT

Tumours of the glomus jugulare

Case report and anaesthetic management for the combined two stage operation

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Summary

Two cases are reported using a two stage procedure for the excision of glomus jugulare tumours. The anaesthetic problems which this may produce are discussed, and recommendations are made regarding the anaesthetic conduct for this procedure. A two stage, combined procedure is suggested to reduce anaesthetic morbidity.

Key words

Tumour; glomus jugulare.
Anaesthesia; hypotension, general.

Glomus jugulare tumours arise from the glomus bodies around the temporal bone and are associated with the jugular bulb adventitia.[1] The glomus bodies are similar, histologically, to carotid bodies, being epithelial cells in a capillary network and encapsulated in fibrous tissue. Unlike the carotid bodies, glomus bodies appear to be functionless,[2] but there have been suggestions that they may act as chemoreceptors, responding to changes in $Pa\text{CO}_2$ and $Pa\text{O}_2$.[3]

Tumours of the glomus body generally arise from the jugular bulb and are histologically benign. However, malignant change has been noted.[4] These tumours are slow growing whether benign or malignant but they invade surrounding structures and extend intracranially to involve the middle and posterior fossae. Inferior extension may also occur and the tumour then becomes apparent as a swelling in the neck.[5] Extension of the tumour down the jugular vein into the superior vena cava is also possible. Glomus tumours are highly vascular; their blood supply is derived from branches of the internal carotid artery.

The symptoms produced by these tumours are caused by their vascularity and the slowly progressive involvement of surrounding structures. Invasion of the middle and inner ear results in tinnitus and hearing loss with or without vestibular dysfunction. Marked vascularity of the tumour may give rise to pulsatile tinnitus.[6] Involvement of the cranial nerves may occur, particularly the VIIth nerve, resulting in facial weakness. Invasion of the skull base may cause IXth, Xth, XIth and XIIth nerve pareses. Intracranial extension of the tumour may produce cerebellar or brain stem involvement, or pareses of the Vth and VIth cranial nerves. Compression of the Sylvian aqueduct may occur with posterior fossa involvement, producing hydrocephalus.[7]

Glomus body tumours, though normally nonfunctional, may secrete catecholamines, thus producing hypertension and palpitations. Raised adrenaline and noradrenaline concentrations

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have been reported in association with glomus tumours,[8] but it is more likely that noradrenaline is the sole catecholamine secreted by these tumours.[5,9,10]

Case histories

Case 1

A 36-year-old man presented with a long history of progressive deafness. He had had a left mastoid exploration, the left being 7 years and the right 4 years earlier. Histology at the time of each operation showed the presence of glomus tumour tissue in both mastoid cavities. He had no hearing in his left ear, but had useful hearing ability, with the help of a hearing aid, in his right ear. He had no other symptoms or signs of neurological disease or involvement. Previous X ray therapy (DXT) on the left side had failed to prevent progressive tumour growth.

Cerebral angiography was performed in order to visualise these tumours radiologically. This procedure was undertaken under general anaesthesia, using thiopentone, pancuronium and fentanyl, with intermittent positive pressure ventilation (IPPV) with 30% oxygen and 70% nitrous oxide and ventilation to normocapnoea. Anaesthesia lasted 2 hours and was entirely uneventful. Angiography revealed the presence of bilateral tumours. The larger of the two tumours was on the left side and had produced extensive bony erosion with tumour in close proximity to the carotid artery and obliteration of the left jugular bulb. The right-sided tumour extended into the tympanic cavity, which was extensively eroded, and was closely approximated to the posterior part of the internal carotid artery.

It was scheduled to remove the tumour surgically with a combined team of ENT and neurosurgeons, using the method described by Fisch.[11] This procedure involves identifying and mobilising the facial nerve, in an attempt to preserve its function, and then to remove the tumour and its supplying vessels in its entirety.

Following premedication with intramuscular papaveretum 20 mg and hyoscine 0.4 mg anaesthesia was induced with thiopentone 300 mg and fentanyl 200 μg. Tubocurarine 45 mg was administered and the trachea intubated using a 9 mm cuffed Oxford tracheal tube. IPPV was instituted using a Manley Pulmovent, with 30% oxygen and 70% nitrous oxide; ventilation was adjusted to maintain an end tidal carbon dioxide concentration between 3.3 and 3.5%. Supplements of tubocurarine and fentanyl (to a total of 125 mg and 350 μg respectively) were added and 1% enflurane was administered throughout the procedure.

Venous access was secured with two 16 swg intravenous cannulae for fluid therapy, and a 16 swg long line via the left antecubital fossa, attached to a saline manometer. A radial artery cannula was inserted to measure arterial pressure. The ECG and nasopharyngeal temperatures were also continuously displayed. The patient was placed on a warming mattress and was surrounded in a foil space blanket.

The operative procedure involved re-opening and enlarging the left mastoid cavity, exposing and ligating the sigmoid sinus and then identifying the facial nerve. This was mobilised and rerouted and the external carotid, ascending pharyngeal and occipital arteries ligated. By this stage, the patient had been anaesthetised for almost 10 hours and many more hours of surgery were anticipated. It was therefore decided to secure haemostasis and close the wound and to proceed with definitive tumour excision the following week.

Throughout this procedure, anaesthesia was uneventful, with a stable blood pressure of 110–130 mmHg systolic and a core temperature of around 35°C. A total of 4 litres of Hartmann's solution and 2 units of whole blood were administered during surgery. Neuromuscular blockade was reversed with atropine and neostigmine and the patient returned in a stable condition to the ward.

Seven days later, the second stage of the procedure was undertaken, with premedication, anaesthesia and monitoring as before. The jugular vein was ligated and followed up to the base of the skull; the tumour was then excised in its entirety. There was no intracranial extension of the tumour, therefore dura was not opened. During this second stage, a total of 120 mg tubocurarine and 600 μg fentanyl were used incrementally, with a supplement of 1% enflurane throughout the procedure. Arterial blood pressure was maintained between 110 and 140 mmHg systolic and core temperature was stable between 35.5 and 36°C. A total of 3 litres Hartmann's solution, 1 litre of 0.9% saline and 3 units of whole blood were infused throughout this procedure. The total anaesthetic time was 7 hours and, again, neuromuscular blockade was reversed and the patient returned to the ward in a stable condition. The two stages of the surgery took almost 17 hours and the patient received 8 litres of crystalloid solution and 5 units of blood.

A persistent cerebrospinal (CSF) leak delayed the patient's discharge from hospital, but he returned home 25 days after surgery. Twelve months later he still has a left-sided VIIth nerve palsy.

Case 2

A 53-year-old woman presented with a 9-year history of progressive left-sided deafness which had not improved despite insertion of grommets. Over the year prior to neurosurgery, she had noticed numbness of the left arm and leg without motor symptoms. Three months before her admission, she had had a polyp removed from her left external auditory meatus which had proved, histologically, to be a glomus tumour. She had experienced no headaches, tinnitus or vestibular disturbance. Angiography one month prior to neurosurgery, revealed the presence of an unusually nonvascular glomus tumour with considerable extension into the middle fossa, but little evidence of bone destruction. In addition, there was occlusion of the left jugular bulb and sigmoid sinus, with abnormal venous drainage through the deep cervical veins. Anaesthesia for the angiography used a conventional relaxant–IPPV technique with fentanyl supplements and ventilation with 30% oxygen in nitrous oxide to maintain normocapnoea and was uneventful.

In view of the radiological findings, she was scheduled to have a combined ENT/neurosurgical excision of the tumour. As it was expected to be a prolonged procedure, and as the technique had proved successful in the first case described, a two-stage procedure was planned, with an interval of 7 days between operations.

For the first procedure she was premedicated with oral diazepam 10 mg 1.5 hours prior to arrival in the anaesthetic room. She was anaesthetised as described previously and her trachea intubated with a cuffed 8 mm Oxford tracheal tube. Monitoring was as for that in case 1 and anaesthesia was maintained with isoflurane 0.5%. The total dose of tubocurarine used was 115 mg, and that of fentanyl 500 μg. Moderate hypotension was maintained using trimetaphan by infusion throughout the procedure, to improve the surgical field and reduce blood loss. The arterial blood pressure was maintained between 80 and 90 mmHg systolic and the heart rate remained steady at 70–80 beats/minute. The surgical procedure aimed, as in case 1, to mobilise and reroute the facial nerve. In addition, a radical mastoidectomy was performed, along with removal of the tympanic membrane and ossicles and cochlea. The facial nerve was decompressed and mobilised and tumour excised from the Eustachian tube. The jugular vein was ligated and removed up to the level of the jugular bulb. At the end of the procedure, neuromuscular blockade was reversed and the patient was transferred, breathing spontaneously, to the intensive care unit (ICU) for overnight observation. Her condition remained stable and she was transferred to the ward the following morning. The total anaesthetic time for this procedure was 9.5 hours and 3 litres of Hartmann's solution was infused plus 2 units of whole blood.

After 7 days the second stage of the surgical procedure was undertaken The petrous bone was drilled to expose the sigmoid sinus. The extracranial portion of the tumour was excised, the dura opened and the intracranial extension of the tumour removed up to the cerebellar–pontine angle using an ultrasonic surgical aspirator. Anaesthesia for this procedure was identical to that for the first. Incremental boluses of fentanyl to a total of 400 μg and tubocurarine to 120 mg were given. Hypotension was again employed using isoflurane 0.5–1.0% and trimetaphan by infusion to maintain a systolic blood pressure of 90–100 mmHg. Intra-operative fluids given were 1 litre of Hartmann's solution and 1 litre of 0.9% saline and the anaesthetic time for this second stage was 7 hours.

At the end of the procedure, neuromuscular blockade was reversed with atropine and neostigmine and the patient extubated and transferred to the ICU for overnight observation. Thirty minutes after arriving in ICU her breathing became laboured and shallow and a marked bradypnoea ensued. The trachea was therefore, reintubated and her lungs electively ventilated overnight. Concurrently, she developed marked hypertension (200/100 mmHg) with a tachycardia. This settled with sedation, and intermittent boluses of labetalol. An urgent CT scan revealed no intracranial pathology to account for her sudden deterioration. The following morning she was stable and alert. Therefore she was extubated and returned to the ward. Six months later she is well, but with a dense left facial nerve palsy necessitating tarsorrhaphy.

Discussion

The incidence of glomus jugulare tumours is very low and these two cases were the first to have corrective surgery performed in Leeds. Most series are therefore small and the anaesthetic management for this procedure has not been well documented. These tumours are very slow growing and treatment may be delayed for years before any symptoms occur. There are reports of patients surviving for 20–40 years without treatment following diagnosis of the condition.[4,7] As the tumour grows, extension into surrounding structures produces cranial nerve involvement, bony erosion, tinnitus and progressive deafness. Surgical excision is, therefore, the treatment of choice to eradicate the disease. X ray therapy has been employed, but this is usually reserved for those patients who are a poor risk for surgery and in those patients whose tumours are extensive.[13,14]

The procedure of surgical excision of glomus jugulare tumours is prolonged. Ghani *et al.*[8] in a recent review on this subject, indicate that the duration of a single stage resection in their series varied from 3–17 hours; our two cases were also prolonged, each taking over 16 hours. It is essential, therefore, to minimise heat loss and avoid pressure on the patient's shoulders and buttocks.

Despite these tumours being relatively small, their close proximity to major vessels and their inherent vascularity predisposes to excessive blood loss. Ogura *et al.*[5] transfused up to 14 litres of blood in their series, and Ghani *et al.*[8] report a range of transfusion between 0 and 10 units. With bony erosion by the tumour, and intracranial extension, a large amount of bone drilling and curetting may be required. The continual ooze from the bone will produce an insidious loss of blood which may be extensive. Indeed, Brown[5] reported a case in which bone blood loss was so large that surgery had to be abandoned. It is important, therefore, to be aware of the potential for a large blood loss, and to take appropriate precautions. The use of a hypotensive technique will reduce bleeding and provide a clearer operating field.

In our first case report, a hypotensive technique was not employed. Despite this, the total blood replacement required was only 5 units. This is not a large volume when compared to other series, but it is, nevertheless, a substantial loss considering the small tumour size. Following this experience, a deliberate hypotensive technique was employed for the second case. Moderate hypotension (80–90 mmHg) produced good operating conditions and blood loss for both stages was only 2 units.

The use of trimetaphan has the disadvantage that the pupillary dilatation produced can interfere with postoperative neurological assessment. Tachyphylaxis and tachycardia are not infrequently seen when using this agent. Sodium nitroprusside has been used for such procedures and Ghani *et al.*[8] recommended this as their agent of choice. Nitroprusside may raise intracranial pressure due to intracranial vessel dilatation.[16] Rebound hypertension on stopping this agent may also be a problem. Furthermore, as the surgical procedure is so prolonged, the theoretical possibility of cyanide toxicity exists, if nitroprusside is used as the sole hypotensive agent. Glyceryl trinitrate also causes marked increases in intracranial pressure and is not recommended where intracranial spread of the tumour is suspected.[17]

Isoflurane causes little or no myocardial depression[18] and produces a dose-related hypotension by decreasing systemic vascular resistance whilst maintaining cardiac output.[19] Its low solubility in blood allows rapid changes in the degree of hypotension produced, with simple manipulation of the inspired concentration. Similarly, rapid washout on withdrawal of the agent allows the blood pressure to return to normal. Little or no increase in intracranial pressure is produced, even at high inspired concentrations, assuming a slightly lowered $P\text{aCO}_2$. The use of isoflurane as the sole hypotensive agent for these cases has much to commend it.

The positioning of the patient with a slight head up tilt, by enhancing cranial venous drainage, further reduces blood loss from the operative site. With the patient in a head up position, surgical procedures in close proximity to major neck veins and intracranial sinuses carries the risk of air embolism. In the two cases reported, the jugular vein was ligated before tumour excision, thus reducing the likelihood of air embolism. Nevertheless, given the potential for such a possibility, appropriate precautions should be considered.

We believe that the benefits from a two stage procedure outweigh the logistic problems in organising surgeons, anaesthetists and theatres. Any subsequent glomus jugulare tumour excision performed in Leeds will be planned this way.

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CASE REPORT

Management of a glomus jugulare tumour with internal carotid artery involvement

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Summary

A previously healthy 40-year-old female presented for surgical resection of a large glomus jugulare tumour with extensive involvement of the carotid siphon and intracranial extension. Conduct of anaesthesia with specific reference to cerebral protection is discussed. A combination of induced hypothermia, barbiturate therapy, normotension, normocarbia and prior clamping of the distal internal carotid artery was chosen. The role of barbiturates as a therapeutic intervention is debated.

Key words

Anaesthetic management; glomus jugulare tumour.
Cerebral protection; hypothermia, barbiturates.

Glomus bodies are paraganglia of neural crest origin which occur in relation to the autonomic nervous system. They occur at a variety of sites, but are microscopically identical. The glomus jugulare arises from a constellation of glomus bodies occurring within the temporal bone. These bodies are situated at the dome of the jugular bulb, on the promontory in the middle ear and in the intrabony canaliculi of the auricular and tympanic nerves.[1]

Glomus jugulare tumours arising at the jugular bulb may present with a variety of caudal cranial nerve palsies due to involvement of these nerves with tumour at the level of the jugular foramen. Continued extension of the tumour to the ear gives rise to otological symptoms. Invasion may progress into the petrous temporal bone, the base of the skull, and finally intracranial extension may occur. The blood supply of the glomus jugulare tumour is derived from the external carotid artery, but very extensive tumours may also have supplying vessels from the internal carotid artery.

Glomus tumours are usually slow-growing neoplasms. The clinical history commonly spans several years.[2–4] The management of this tumour is a team project, involving radiologists, surgeons and anaesthetists. During the surgical

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extirpation of a glomus jugulare tumour with intracranial extension and internal carotid artery involvement, the anaesthetist is required to provide conditions and administer drugs which may protect the brain either prior to an ischaemic event, or possibly soon after such an event has occurred. The combined effect of unilateral internal carotid artery sacrifice and sudden severe blood loss can result in ischaemic brain damage.

Case history

A 40-year-old Caucasian woman weighing 60 kg was scheduled for surgical removal of a glomus jugulare tumour. She presented with a 7-year history of progressive vertigo and tinnitus, and a 6-month history of deafness in her right ear. Examination revealed a pulsatile red–blue tumour behind her right tympanic membrane. Computerised tomography[5,6] and carotid angiography[5] confirmed a large vascular tumour of the jugular bulb extending into the posterior fossa and the cavernous sinus via the carotid canal in the base of the skull. The wall of the right internal carotid artery was involved with tumour in the carotid canal segment. Crossover blood flow from left to right across the circle of Willis was adequate.

In spite of the extent of tumour spread, it was decided that surgery was justified in view of the very poor ultimate prognosis offered by alternative therapy. It was proposed to open the cranium and clip permanently the right internal carotid artery just proximal to its bifurcation into anterior and middle cerebral arteries. This was to be followed by proximal ligation of the right internal carotid artery and right internal jugular vein in the neck, which were to be removed together with the tumour and most of the right petrous temporal bone.

At the pre-operative visit, the patient was assessed to be ASA rating 1. She was deaf in the right ear, and had decreased labyrinthine function, decreased facial nerve function and vagal, accessory, glossopharyngeal and hypoglossal palsies due to tumour invasion. Investigations, including full blood count, urea and electrolytes, bilirubin, alkaline phosphatase, SGOT and SGPT, chest X ray and ECG were all within normal limits. A 24-hour urine collection for vanillyl-mandelic acid (VMA) as a screening test for catecholamine production was normal.

Premedication consisted of intramuscular papaveretum 10 mg and promethazine 25 mg, given one hour pre-operatively. The patient was placed on a warming/cooling blanket. Monitoring included ECG, retrocardiac oesophageal temperature, capnograph, central venous and radial arterial pressures and urinary output. Half hourly arterial blood gas analyses were performed and corrected for hypothermia.

Anaesthesia was induced using thiopentone 300 mg followed by pancuronium 6 mg and the patient intubated with a 8.0 mm cuffed nasal tracheal tube. Her lungs were ventilated with an expired minute volume of 6 litres and a frequency of 12 breaths/minute. Anaesthesia was maintained with nitrous oxide, oxygen and enflurane 0.6%, with a fractional inspired oxygen concentration of 0.4. During the course of the procedure, carbon dioxide was added to the inspired gas at a flow of 200 ml/minute to maintain $P\text{aco}_2$ at approximately 4.6 kPa. With the onset of anaesthesia, surface cooling was commenced, using a cooling blanket and intermittent placement of ice packs in the groins and axillae. The patient was cooled to a retrocardiac oesophageal temperature of 30°C. At the time of ligation of the intracranial portion of the right internal carotid artery, the oesophageal temperature was 32°C.

During the hour prior to intracranial carotid clamping, an infusion of thiopentone 1 g was given; in the 2.5 hours following internal carotid artery ligation, a further 33g thiopentone was infused. In addition, the patient received 300 mg hydrocortisone intravenously. Mannitol 20 g was administered to improve operative conditions for neurosurgery.

The systolic blood pressure prior to induction was 120 mmHg and thereafter with minor variations, was maintained at 100 mmHg for the duration of the procedure. On two occasions a drop in systolic pressure to 80 mmHg responded rapidly to a titrated dose of cafedrin—HCl with theodrenalin—HCl (Akrinor). The pulse rate which was 80 beats/minute pre-operatively, was maintained at 60 beats/minute throughout the procedure. On two occasions, the pulse rate dropped below 60 beats/minute, and did not respond to administration of atropine 0.5 mg intravenously on either occasion. The central venous pressure was maintained between 6 and 9 cm H_2O.

Arterial blood gases remained normal, as did serum urea and electrolytes. A steady urine output over the 12 hours in the operating room totalled one litre. Blood loss estimated by swab weight was 4.5 litres, and this was replaced with whole blood 3.5 litres, freeze dried plasma one litre and fresh frozen plasma 750 ml. In addition, a total of 4.2 litres Ringer lactate was infused.

The patient was gradually rewarmed over several hours and electively ventilated for a further 10 hours. For a period of 10 days postoperatively she was confused and experienced paranoid delusions, but gradually regained her normal mental state. There were no electrolyte changes postoperatively. This confusion was thought to be due to subfrontal retraction which is often associated with confusion for several days postoperatively. She has a permanent right facial nerve palsy due to excision of an involved proximal segment of the facial nerve, but no additional cerebral neurological deficit. She continues to be well 4 years postoperatively, with no demonstrable tumour recurrence. She has not had aspiration problems as a result of her continuing unilateral vagal nerve palsy.

Discussion

The major problem in the anaesthetic management of a paraganglioma of the jugular bulb with involvement of the ipsilateral internal carotid artery is to ensure adequate cerebral protection consequent upon sacrificing the internal carotid artery. This was the cause of fatality in at least one reported case in which resection of an internal carotid artery with subsequent vein grafting led to massive cerebral infarction.[7] The anaesthetic management of two patients undergoing resection of carotid body tumours has previously been described.[8,9]

In our patient, angiography[5] had revealed adequate crossover flow via the left internal carotid artery and vertebrobasilar systems to the right cerebral hemisphere. Maintenance of this flow was imperative. We attempted to achieve this by ensuring normocarbia at all times by the addition of carbon dioxide to the inspired gases during the period of hypothermia. This would assist in preventing cerebral vasoconstriction due to lowered arterial carbon dioxide tension subsequent to the induced hypothermia.[10]

Initial intracranial clamping of the right internal carotid artery just proximal to its bifurcation into the anterior and middle cerebral arteries was carried out in order to prevent the problem of cerebral ischaemia due to haemorrhage from the distal internal carotid artery stump in the carotid canal during removal of the tumour with its associated major blood vessels. The significant haemorrhage from the distal internal carotid artery stump is reduced by the prior internal carotid artery clamping. This avoids ischaemia due to reduced cerebral blood flow during the period of distal internal carotid artery stump haemorrhage. The steal from the transiently open distal internal carotid artery stump through the posterior communicating artery is a minor problem and is easily controlled by gentle packing.

Because surgery for this highly vascular tumour may be associated with sudden severe haemorrhage and concomitant hypovolaemia, preplanned cerebral protection using hypothermia and barbiturates was used to minimise possible brain damage. It is well known that the glomus jugulare tumour draws collateral arterial supply through the carotid canal and cavernous sinus dural arterial branches of the internal carotid system. This causes significant bleeding, which may lead to cerebral damage, despite the prior internal carotid artery clamping.

Anaesthesia was performed at an altitude of 5750 feet (1750 metres) above sea level. An important anaesthetic consideration at moderate altitude in patients undergoing neurosurgical manipulation relates to the definition of the normal $P\text{aco}_2$ value. At moderate altitude, (5000 to 10 000 feet above sea level) with the decrease in barometric pressure and relative hypoxia, there is a progressive increase in minute ventilation and, consequently, a reduction in the normal $P\text{aco}_2$ to 4.80 kPa at 5000 feet[11] and 4.67 kPa at 5750 feet.[12] Maintenance of normocarbia at this altitude during hypothermia was ensured by the addition of carbon dioxide to the inspired gas mixture at a flow of 200 ml/minute.

It is well known that hypotension causes failure of the cerebral collateral circulation[13,14] and therefore normotension was maintained throughout the procedure. The survival of focally ischaemic cerebral tissue is suggested to depend upon the maintenance of a critical balance between cerebral blood flow and metabolism.[15]

Barbiturate therapy has been advocated for cerebral protection during a period of ischaemia. Clinical evidence of the usefulness of barbiturates in affording cerebral protection is at present both contradictory and anecdotal. However, there are useful clinical applications for barbiturate therapy in circumstances analogous to the animal stroke models.[16,17] It is in the model of focal cerebral ischaemia that barbiturates appear to offer the greatest protection.[18] In some of these models, it has been found that the brain does not infarct immediately following the occlusion of a single major vessel, and irreversible damage may not occur for several hours depending on collateral flow.[19] The magnitude of protection afforded by barbiturates during this period of ischaemia is assumed to be related to the metabolic depression induced by the drug, as well as to delay in the development of membrane failure with ischaemia.[20,21] Barbiturates thus decrease membrane excitability and impulse traffic, and thereby decrease high energy phosphate adenosine triphosphate (ATP) requirements. The major undisputed mechanism of action has been postulated to be related to improvement in the ratio of oxygen supply to oxygen demand.[22,23] The finding that the 50% ATP depletion level during ischaemia may be delayed from 60 to 120 seconds by pre-ischaemic barbiturate coma in rats may constitute another indication for thiopentone.[24] The action of barbiturates in protecting against cerebral ischaemia by scavenging of free radicals is unlikely.[25] Barbiturate cerebral protection may, however, be a function of the anaesthetic action of barbiturates and the accompanying cerebral metabolic depression rather than a function of the barbiturate molecule itself.[18,26] A combination of mechanisms is thus proposed to provide cerebral protection.

The barbiturate dosages, their timing and duration of administration vary widely. It has been demonstrated that thiopentone was effective in decreasing the neurological defects and infarct sizes in dogs when administered before and after focal ischaemia produced by occlusion of the middle cerebral artery.[27] Thiopentone 30 mg/kg was administered to provide cerebral protection 5 minutes before circulatory arrest to patients undergoing aortic arch aneurysm repair under deep hypothermia and circulatory arrest.[28] The intra-operative thiopentone dose in humans has varied from 2-75 mg/kg.[15]

Our patient received a thiopentone infusion of 30 mg/kg, which commenced one hour prior to intracranial internal carotid artery clamping and was completed 30 minutes after the clamping. Our intention was to complete the 30 mg/kg infusion prior to internal carotid artery clamping, but haemodynamic instability necessitated slowing the infusion, together with fluid and colloid administration, to ensure normotension. Our patient therefore received thiopentone 17 mg/kg during the hour prior to internal carotid artery clamping, 20 mg/kg during the next hour and 17 mg/kg in the hour thereafter. Careful titration ensured the maintenance of normal systemic arterial pressure which has been suggested to be as valuable as most forms of drug therapy.[29]

The potential for cerebral protection using moderate hypothermia with reduction in brain temperature to 30°C is well established.[18] There is good reason to believe that induced hypothermia, by significantly reducing the metabolic rate, will increase tolerance to a period of ischaemia. Induced hypothermia was thus employed as an additional means of providing cerebral protection.

The use of steroids as an adjunct in cerebral protection prior to or during focal ischaemia is controversial, although various mechanisms of action including membrane stabilisation, inhibition of lysosomal enzyme release and free radical scavenging have been proposed.[30] Membrane stabilisation of the blood–brain barrier is not relevant during the critical stages of cerebral oedema secondary to cerebral ischaemia.[31] There is no conclusive evidence supporting the beneficial effect of steroids. The hydrocortisone administered to our patient possibly served no useful purpose; the preferred agents are dexamethasone or methylprednisolone.[28,32] The induced hypothermia produced sinus bradycardia, which was unresponsive to atropine administration.

The combination of induced hypothermia and barbiturate therapy to provide cerebral protection was associated with the successful excision of an extensive jugular paraganglioma with intracranial extension and internal carotid artery involvement. There still remains a role for barbiturate cerebral protection employing thiopentone in the operating room situation,[-8] as in the management of a glomus jugulare tumour with extensive intracranial extension and internal carotid artery involvement.

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Anaesthesia, 1986, Volume 41, pages 866–867

APPARATUS

New syringes for arterial blood sampling

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Summary

Two new syringes for arterial blood sampling were compared. Fifty syringes of each type were randomly tested in awake patients and no significant differences were found regarding time taken to collect samples, or the pain experienced by the patient. Air bubbles were found in, and blood leaked, from the Pulsator syringes significantly more often than from the Radiometer B 129 syringes ($p < 0.005$).

Key words

Equipment; syringes.

The management of patients with respiratory insufficiency depends on the reliable measurement of arterial blood gases. The common technique for sampling arterial blood employs a 2–10 ml syringe, into which heparin is drawn from a multiple puncture vial and arterial blood is collected using a 22–25-gauge needle. Blood is collected by manual aspiration of the plunger. Several possible sources of error are inherent in this technique: the dilution of the sample by heparin, difficulty in keeping the needle in position while aspirating the plunger, the possibility of aspirating venous blood or air bubbles into the sample and the risk of contamination from the multiple puncture heparin vial.

We have evaluated two new single-use preheparinised syringes, designed to eliminate these sources of error. The Pulsator* syringe uses a low friction plunger, which allows the arterial pressure to raise it to a certain point, without the use of manual aspiration. It contains a solution of heparin. The Radiometer† syringe has a number of grooves at the upper end of the inner surface of the syringe at the position 'open', allowing air to escape with the plunger in this position. It contains heparin as a dry tablet.

Methods

Fifty syringes of each kind were randomly used in patients who, due to their clinical condition, were to have arterial blood gas analysis performed. Only one sample was taken from each patient at a time. All patients described the degree

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*Concord Pulsator 910/400/380, manufactured by Concord Laboratories Ltd, Park Farm Road, Kent CT 19 5DR, U.K.

†Radiometer 956-286, manufactured by Radiometer A/S, Emdrupvej 72, DK-2400 Copenhagen NV, Denmark.

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of discomfort or pain at the time of arterial puncture on the visual analogue scale. The time taken for sampling, the occurrence of air bubbles in the syringe after sampling and any leakage of blood from the syringe before a protective cap could be placed over the needle were recorded. All the punctures were performed by two registrars (T.W. and P.B.) and the samples were drawn from the radial artery.

Results

The results are summoned in Table 1. The time taken for the sampling procedure (median 50 versus 55 seconds) and the reported pain associated with the sampling (median 5.2 arbitrary pain units on a visual analogue scale in both groups) were equal in the two groups (using the Mann-Whitney rank sum test). However, bubbles of air were found in 27 samples in Pulsator syringes compared to seven samples in Radiometer syringes. Furthermore, blood leaked from 13 Pulsator syringes but only from one Radiometer syringe before a protective cap could be placed on the syringe after sampling. These differences were statistically significant at $p < 0.005$ using the Chi squared test with Yates' correction.

Table 1. Comparison of two syringes for arterial blood sampling

	Pulsator $n = 48$	Radiometer $n = 50$	Difference
Time for sampling* (seconds)	55 (40–70)	50 (25–65)	N.S.
Pain* arbitrary units 0–10	5.2 (5.0–7.2)	5.2 (5.0–7.0)	N.S.
Leaks	13	1	$p < 0.005$
Air bubbles	27	7	$p < 0.005$

* Figures given are median values (interquartile range). N.S.: Not significant.

Two Pulsator syringes were found to clot in the needle during identification of the artery. This effect was not encountered using the Radiometer syringes.

Discussion

Arterial blood sampling for gas analysis may be done with syringes made of polypropylene and achieves the same results as with glass syringes.[1] No variation is found when using different needle sizes.[2] However, a common source of error is dilution of the sample by heparin which may seriously alter the $P\text{CO}_2$ and pH.[3,4] The use of preheparinised syringes eliminates this problem. Bubbles of air in the sample artificially raise the $P\text{O}_2$ and lower the $P\text{CO}_2$.[5] If bubbles are expelled from the sample within 2 minutes of sampling, they will not significantly affect the blood gases but will probably result in some contamination with blood. AIDS with associated frequent severe pulmonary infections, has resulted in the need to eliminate the risk of contamination by blood. The reason for the leakage of blood from the Pulsator syringes may be that the pressure within the sample, at the moment the needle is removed from the patient, is the arterial pressure, whereas the Radiometer syringe is at atmospheric pressure, due to its different construction.

In conclusion, we consider that the use of preheparinised syringes for arterial blood sampling represents a useful development in the clinical determination of blood gases. We found that the Radiometer B 129 syringe had advantages for this purpose, and it is 33% cheaper than the Pulsator.

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Anaesthesia, 1986, Volume 41, pages 868–869

Forum

Psychomotor testing of on-call anaesthetists

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Summary

The critical flicker fusion frequency and choice reaction times of 16 on-call anaesthetists were measured between 1400 and 1600, at 2300 and at 0200 hours. Critical flicker fusion decreased between the afternoon and 2300; there was no further change between 2300 and 0200. No significant differences in choice reaction times were found on any of these different occasions.

Key words

Anaesthetists; fatigue.
Measurement techniques; critical flicker fusion frequency, choice reaction time.

It is generally agreed by the profession that the practice of anaesthesia requires maintenance of vigilance for prolonged periods of time.[1,2] Compared with other branches of medicine, the results of human error can potentially result in damage to patients in a very short period of time. Some studies have investigated 'near misses' during anaesthesia,[3,4] and mention tiredness and relaxed vigilance as a possible factor in these events. Not surprisingly, virtually all anaesthetists admit to subjective feelings of tiredness during the early hours of the morning. However, it is difficult to say to what extent, if any, this impairs their ability to conduct safe anaesthesia. With this in mind, the aim of this study was to investigate the higher functions of on-call anaesthetists during the day and at night using two objective tests of neurological performance.

Method

Sixteen on-call junior anaesthetists were studied on three sequential occasions during the day, i.e. between 1400 and 1600 hours, at 2300 hours and at 0200 hours. All had visual acuities of at least 6/6; subjects retained their spectacles if worn. None were taking any psychotropic drugs, and all had been asked to refrain from caffeine or nicotine intake for 2 hours before the test. Lighting and test conditions were standardised by conducting measurements in an unused, windowless anaesthetic room.

Critical flicker fusion frequency (CFFF) and choice reaction time were measured using the Leeds psychomotor tester.[5] The critical flicker fusion frequency apparatus consisted of a flashing light of wavelength around 550 nm which the subject observed from one metre. The flicker frequency of this source was increased from 12 Hz at a rate of 1 Hz/second. The end point occurred when the subject discerned that the flickering light became continuous. This was repeated three times. Three further measurements were taken as the flicker frequency was reduced from 50 Hz and the subject asked to discern when the source started to flicker. An average reading was then calculated from the six results obtained.

In order to measure choice reaction times (CRT) the apparatus required the subject to move his finger from a central button to one of six peripheral buttons as quickly as possible. A light adjacent to each peripheral button lit up randomly, thus indicating to the subject which button he was required to press. Two times were measured, that from illumination of the light to release

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of the central button (CRT1), and that from release of the central button to contact with a peripheral button (CRT2). The times from thirty attempts were averaged.

Statistical comparison of the data obtained was made by means of a paired Student's *t*-test.

Results

Table 1 shows the results obtained at the different times. Mean afternoon CFFF was 35.2 Hz; this was reduced by 2.4 and 2.0 Hz at 2300 and 0200 hours respectively.

Table 1. Mean values (SEM) of CFFF, CRTI and CRT2 between 1400 and 1600, at 2300 and at 0200 hours ($n = 16$)

	CFF	CRTI	CRT2
1400–1600	35.2 (0.54)	0.37 (0.016)	0.18 (0.011)
2300	32.8 (0.72)*	0.37 (0.011)	0.18 (0.014)
0200	33.2 (0.48)*	0.40 (0.018)	0.19 (0.014)

*$p < 0.001$ significant difference from 1400–1600 hours.

At 2300, four of the junior staff showed no reduction in CFFF, and three of these still maintained this performance at 0200. Values for CRT showed an upward trend as the day continued, but this was not significant. However, in two individuals CRT1 and CRT2 were prolonged by a factor of more than 0.2 and 0.1 seconds at 0200. At this time, CFFF was decreased by more than 4 Hz in these two subjects.

Discussion

Critical flicker fusion frequency and choice reaction time have been widely used by clinical psychologists to investigate psychomotor function in humans.[6,7] It appears to be a sensitive measure of the level of arousal of subjects, whereas CRT gives an indication of psychomotor performance, i.e. the coordination of sensory and motor systems. A lowering of CFFF and a prolongation of CRT occur after the administration of sedative drugs, and opposite effects occur after ingestion of amphetamines.[6]

The daytime value of 35.2 for CFFF which we obtained is similar to that reported by Whitwam *et al.*[8] Compared with the changes we detected during the day, reported decreases in CFFF one hour after a single dose of diazepam 10 mg, lorazepam 2.5 mg or pethidine 75 mg, are 2.5 to 4 Hz, 4 Hz and 5 Hz respectively.[9,10] Not all of our subjects displayed the same level of impairment; indeed, four showed no decrease in CFFF at 2300 and, of these, three still showed no reduction at 0200. This seems to give credence to the idea that a proportion of people can continue well into the night without suffering fatigue. Compared with results after benzodiazepine administration,[10] there were no significant differences in CRT at the different times. However, two individuals did show marked prolongation in their CRT at 0200, and in these subjects the CFFF was reduced to a greater extent than that in the group as a whole.

This study indicates that, in general, arousal levels of most on-call anaesthetists are impaired by 1100 at night, but no further impairment occurs after this time, up to 0200. On the other hand, psychomotor performance, as assessed by choice reaction time, is unimpaired at these hours in the great majority of anaesthetists.

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Oral lormetazepam in premedication. A comparison with diazepam

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Summary

Lormetazepam, a relatively new benzodiazepine was compared in a randomised, double blind trial with diazepam for its effectiveness as an oral premedicant drug. A scoring system was used to assess sedation, relief of anxiety, nausea, dizziness and cardiovascular effects in two groups of patients having orthopaedic operations. Some statistical indication that lormetazepam has a greater anxiolytic effect than diazepam was found, but in assessing total effect using a known scoring system, no difference was demonstrated between the two drugs.

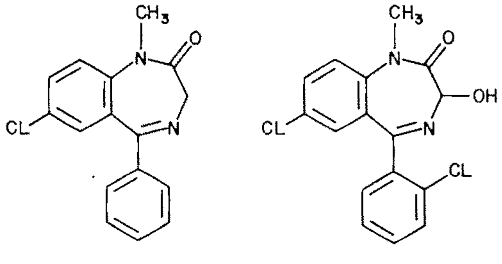
Key words

Premedication; benzodiazepines, diazepam, lormetazepam.

Benzodiazepines are widely used in premedication for their sedative and anxiolytic properties. Recent trends towards the use of oral premedication and towards day case surgery have aroused interest in benzodiazepine drugs with shorter half lives and without active metabolites.

Lormetazepam is a new derivative belonging to the benzodiazepine group;[1] its main characteristic is the methyl group at the 1-position of the diazepine ring (Fig. 1). It was introduced as a hypnotic drug and comparative studies with other benzodiazepines have shown it to be superior in this respect to diazepam.[2] Pharmacokinetic studies have shown rapid and complete absorption from the gastrointestinal tract and an elimination half life of about 13 hours,[1] compared with diazepam which has a half life of about 50 hours.[3]

These properties suggest it to be a suitable alternative for use as an oral premedicant in anaesthetic practice.



Diazepam

Lormetazepam

Fig. 1. The chemical formula for diazepam and lormetazepam

For convenience, and because the dose–response curves of the benzodiazepines are relatively flat, anaesthetists often prescribe a single dose for premedication in adults of widely ranging body weights.[4,5]

The present double blind trial was carried out to determine the effectiveness of lormetazepam in comparison with diazepam.

Method

Fifty patients were allocated at random to one of two groups. The groups were comparable for age, sex, blood pressure and heart rate and consisted of patients of ASA grades 1 and 2 scheduled for orthopaedic operations (Table 1). All patients gave informed consent according to the Helsinki II declaration and the study was approved by the local scientific ethical committee. Five patients were excluded from the series because their operations were cancelled.

Patients in group 1 received diazepam 15 mg, those in group 2 received lormetazepam 2 mg, 1.5–3 hours before surgery. Both drugs came from coded, individual envelopes. The drugs were given by nursing staff and the observers had no knowledge of which drug had been administered. Observations were carried out in the ward before administration of the tablets and in the anaesthetic room before induction of anaesthesia. Effects of the drugs were evaluated using a modification of the method described by Dundee *et al.*[6] and, later, by Chalmers and Horton[7] (Table 2 and 3).

Observations were made of the degree of sedation and anxiety of the patient, the presence or absence of nausea and dizziness and cardiovascular effects (non-

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Table 1. Demographic data. Mean (SEM)

	Diazepam	Lormetazepam
No. of patients	23	22
Age (years)	34 (7)	31 (9)
% male	47.8	36.4
Blood pressure (mmHg)		
Systolic	126 (15)	124 (14)
Diastolic	77 (10)	78 (11)
Heart rate (beats/minute)	73 (12)	73 (11)

Table 2. Scheme for scoring the effects of premedication (modified from Dundee *et al.*[6] and Chalmers and Horton[7])

Desired effects criteria	Score	Adverse effects criteria	Score
Good sedation with relief of anxiety	+5	Patient unmanageable or severe cardiovascular effects with or without other adverse effects	−5
Good sedation with partial relief of anxiety or fair sedation with relief of anxiety	+4	Moderate cardiovascular effects with or without dizziness and nausea	−4
Slight or no sedation with relief of anxiety or fair sedation with partial relief of anxiety	+3	Slight cardiovascular effects with or without dizziness and nausea	−3
Good sedation with no relief of anxiety or slight or no sedation with partial relief of anxiety	+2	Dizziness or nausea with no cardiovascular effects	−3
No sedation with no relief of anxiety	+1	No cardiovascular effects and no dizziness or nausea	−3
Fair or slight sedation with increase in anxiety			

Table 3. The effects of premedication after assessing and questioning the patients. (The actual effects after premedication)

	Desired effects no. of patients			Adverse effects no. of patients	
	Diazepam	Lormetazepam		Diazepam	Lormetazepam
Sedation			Dizziness		
good	7	6	present	5*	0*
fair	4	5	absent	18	22
slight	8	5			
nil	4	6	Nausea		
			present	1	0
Anxiety			absent	22	22
absent	9*	17*			
slight	9	4	Cardiovascular		
moderate	4	1	arterial blood pressure		
marked	1	0	± 10 mmHg	16	15
			> 11–20 mmHg	4	3
			< 11–20 mmHg	3	4
			Pulse rate ± 10 beats/m	13	14

*$p < 0.025$ (χ^2-test).

invasive measurement of arterial blood pressure and heart rate).

Sedation. The degree of sedation was graded as good, fair, slight or nil. Good sedation was regarded as present if a patient dropped off to sleep when undisturbed. Excessively deep sedation was given a lower score (minus 1 in total score).

Anxiety. The degree of anxiety, after assessing and questioning the patient, was graded as nil, slight, moderate or marked before and after premedication. Relief or aggravation, if any, was noted and scored accordingly. Although this comparison met with some difficulty, it was used for grading total score (Table 2 and 4). In Table 3, the actual degree of anxiety after premedication was used.

Dizziness and nausea. Dizziness and nausea were graded as present or absent.

Cardiovascular effects. The fall in blood pressure (systolic) was graded as nil (0–10 mmHg), slight (11–30 mmHg), moderate (31–40 mmHg) or severe

Table 4. Distribution of scores, Ridits and average Ridit for both groups

	Diazepam		Lormetazepam	
Score	No.	Ridit	No.	Ridit
−4	0		0	
−3	0		0	
−2	4	0.087	0	
−1	2	0.217	4	0.868
0	6	0.319	5	1.595
1	6	0.652	4	2.608
2	2	0.826	6	4.956
3	2	0.913	1	0.913
4	1	0.978	2	1.956
Average ridit		0.500		0.586
Standard error		0.12		0.12
95% CL		0.380–0.620		0.466–0.706

(>40 mmHg). Similarly, a rise in blood pressure was graded as nil (0–10 mm), slight (11–20 mmHg), moderate (21–40 mmHg) or severe >40 mmHg).

An increase in heart rate was graded as nil (0–10 beats/minute), slight (11–40 beats/minute), moderate (40–60 beats/minute) or severe (>60 beats/minute). A decrease in heart rate up to 20 beats/minute was considered beneficial and given $+1$ in the total score (Table 2 and 4). A change in heart rate of less than 10 beats/minute was not considered to be clinically important. A decrease in heart rate was graded as slight (21–30 beats/minute), moderate (31–40 beats/minute) or severe (>40 beats/minute).

The most marked effect on blood pressure and heart rate in any one of the patients was used for the grading and scoring. To facilitate interpretation of the overall effects of the premedication we used the scoring system described by Dundee *et al.*[6] and later modified by Chalmers and Horton[7] to grade desired and adverse effects (Table 3).

The net rating in Table 4 was obtained by subtracting the adverse score from the desired score for each patient (Table 2), thus giving nine categories ranging from $+4$ (good sedation, relief of anxiety and no adverse effects) to -4 (no sedation, no relief or increase in anxiety and severe adverse effects).

Statistical analysis. Ridit analysis was used to determine the degree of significance of observed differences between the two drugs. The diazepam group was considered to be the identified distribution. The actual state after premedication was tested using the Chi squared test. A p value of less than 0.05 was considered significant.

Results

Sedation. Seven patients in the diazepam group and six in the lormetazepam group were scored as being well sedated, one in the diazepam group excessively sedated, while four patients in the diazepam group and seven in the lormetazepam group were not sedated (Table 3).

Anxiety. After premedication, anxiety was absent in nine patients in the diazepam group and in 17 in the lormetazepam group ($p<0.025$, χ^2 test, Table 3). Relief of anxiety was achieved in six patients in the diazepam group and ten in the lormetazepam group, while eight patients in the diazepam group and one in the lormetazepam group were found to be more anxious after premedication ($p<0.01$, χ^2-test). Table 3 shows the 'status' of anxiety after premedication.

Dizziness and nausea. Five patients in the diazepam group complained of dizziness and one of nausea, while none of the patients who received lormetazepam suffered dizziness or nausea ($p<0.025$, χ^2-test, Table 3).

Cardiovascular effects. No patient suffered any severe cardiovascular effects. The average blood pressure before and after premedication was similar in both groups, but some differences were found between the groups with regard to heart rate changes. More patients in the lormetazepam group had raised heart rates, while three patients in the diazepam group were found to have lower heart rates (a decrease of 10–20 beats/minute) compared to none in the lormetazepam group. However, using Ridit analysis, as described by Dundee *et al.*,[6] no significant difference was demonstrated in total score at the 5% level (Table 4).

Discussion

Benzodiazepines have found wide application as sedatives and anxiolytics in medicine generally. In recent years, these drugs have been widely used for premedication precisely because of these properties. Several studies have been published, but only relatively minor differences have been found between the various benzodiazepines.[1,3,4,7]

The main property required in anaesthetic premedication is anxiolysis, as it is known that sedation can mask apprehensive symptoms in patients.[7] We found that more patients in the lormetazepam group were not anxious and that a smaller number of patients showed increased anxiety after premedication. The dosages of 15 mg diazepam and 2 mg lormetazepam were found to be appropriate for premedication in most patients and no severe adverse effects were observed.

The scoring system developed by Dundee *et al.* using Ridit analysis of the results should be able to demonstrate a difference between two groups, if one existed. No such difference was found in this clinical trial, apart from the abovementioned difference in anxiety. This could be because of the design of the scoring system, where the advantage in relief of anxiety was diminished because of the different pattern in heart rates after premedication.

The significant effect of lormetazepam on reduction of anxiety shows that the drug may have some advantage over diazepam in premedication. However, the fact that lormetazepam is somewhat more expensive must be taken into account in any cost–benefit analysis.

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Convulsions after adrenaline administration during enflurane anaesthesia

The tendency of enflurane to cause electroencephalographic high voltage spike activity, spike wave complex with burst suppression and clinical evidences of seizure-like activity are well recognised. However, this has not been reported in relation to the effect of adrenaline administration on seizure activity during enflurane anaesthesia.

A 15-month-old infant, who weighed 9.2 kg, was scheduled for repair of cleft soft palate. The patient was premedicated with atropine 0.1 mg and hydroxyzine 20 mg intramuscularly. Anaesthesia was induced with 50% nitrous oxide and 0.5% enflurane and this concentration was gradually increased to 3.0%. The trachea was intubated, after 20 mg suxamethonium and anaes-

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thesia was maintained with nitrous oxide 50% and enflurane 2.0%. Prior to the operation, 4 ml adrenaline (1:100000 in saline solution) was infiltrated locally in the palate. Five minutes later, the patient had a generalised tonic/clonic convulsion which lasted 15 seconds but required no therapy.

Another 17-month-old infant, who weighed 9.0 kg, was also to undergo repair of cleft soft palate. Preoperative medication included hyoscine 0.1 mg and hydroxyzine 20 mg intramuscularly. Anaesthesia was induced with 67% nitrous oxide and 2.5% enflurane and the tracheal intubation was performed with 20 mg suxamethonium intramuscularly. Fifteen minutes later, 2 ml adrenaline (1:100000 in saline solution) was infiltrated in the palate prior to incision and a tonic/clonic convulsion which lasted 10 seconds occurred.

The third patient was a 16-year-old male who weighed 56 kg, with a low placed spinal conus medullaris, who was scheduled for releasing of the tethering. Premedication included atropine 0.5 mg and hydroxyzine 50 mg intramuscularly. General anaesthesia was induced with intravenous thiamylal 250 mg, followed by suxamethonium 60 mg intravenously for tracheal intubation; the patient's lungs were ventilated with nitrous oxide 50% and enflurane 2.5%. Just after the lumbar subcutaneous infiltration of adrenaline (52 ml, 1:200000 in saline solution) to diminish bleeding at the skin incision, general tonic/clonic convulsions occurred twice, for 15 seconds and 5 seconds, respectively. Blood gas analysis revealed $P\mathrm{ao}_2$ 39.3 kPa torr, $P\mathrm{aco}_2$ 6.2 kPa and pH 7.297.

Postoperative electroencephalogram (EEG) showed no abnormality in these patients. Neigh *et al.*[1] indicated that spike forms and isoelectric periods of EEG were not uncommon with enflurane at clinical concentrations and were potentiated by reduction of $P\mathrm{aco}_2$. With measurement of $P\mathrm{aco}_2$ in only one case and without measurement of enflurane blood concentration in all cases, it is difficult to conclude the effect of adrenaline on seizure activity during enflurane anaesthesia. However, in our three cases, there seemed to be some interaction of enflurane and adrenaline in causing seizures. It is possible that the catecholamine altered enflurane uptake in the central nervous system or the threshold for an enflurane-induced seizure. These three cases suggest that further detailed investigation of the influence of adrenaline during enflurane anaesthesia is needed.

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Depression and anxiety in pain clinics

It was interesting to read the comments of Dr Clarke and Dr Barnes (*Anaesthesia* 1986; **41**: 325–6) on the paper by Dr Hanks and his colleagues (*Anaesthesia* 1985; **40**: 676–9). The Pain Relief Clinic in Newcastle has used screening tests for some time to detect psychiatric illness and psychological handicap.[1,2] The latter study supports the views of Dr Hanks and Dr Lloyd that the General Health Questionnaire[3] (GHQ) is unsuitable for use in a British pain clinic setting and that the Hospital Anxiety–Depression[4] (HAD) scale is likely to be more reliable.

In this study, psychiatric illness was assessed by administration of the Present State Examination[5] (PSE) and a full interview by a consultant psychiatrist. Various screening questionnaires, including the GHQ and the Leeds Self-Assessment Scales for Depression and Anxiety[6] (from which the HAD scale was developed), were evaluated for their ability to detect psychiatric and psychological handicap. The shorter 30-item GHQ is an instrument designed to identify those patients with psychiatric disturbance from a population with somatic illness. Using the recommended cut-off score of over 4 on this questionnaire, 78% of patients in the study were identified as psychiatric. Even with separation at a score of 12, 54% of the patients fell into the psychiatric category, with a diagnostic confidence of less than 60%. This is well in excess of those diagnosed by the PSE. In our population, clearest separation was achieved using a cut-off score of 15 with this instrument, but even with this best discrimination, 34% of the patients were incorrectly classified. This figure fell to 27% using the Leeds Scale, using the optimal cut-off score of 8, one more than the designers of the scale recommend. A full evaluation of the use of the HAD scale is in progress; initial results are similar to those achieved with the Leeds Scale.

Thus it appears that the high incidence of depression mentioned by Dr Clarke and Dr Barnes may be due, in part, to the use of a flawed instrument, although this would be dependent on how they chose to use it. It may also reflect a quite different patient population and it may transpire that the GHQ is eminently suitable for screening patients from the Canadian prairie provinces. Our results suggest that the HAD scale is appropriate for screening a British pain population and it is worth emphasising that an abnormal result is merely an indication that further specialist help should be sought. Assessment of psychiatric and psychological handicap should become routine if the possibility of misdiagnosis and consequent mistreatment is to be avoided.

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A matter of vigilance

We are, I am sure, all agreed that the raising of standards of care in anaesthetics is highly desirable and has been happening in the last few years, with the widespread use of sophisticated monitoring devices and pressure alarm systems. For Dr R.A. Green in his Editorial (*Anaesthesia* 1986; **41**: 129–30) to pick out one item, the physical absence of the anaesthetist from the operating theatre, as the basis for a charge of manslaughter if the patient dies, rather than a general lack of vigilance such as a failure to use properly the many aids available to the anaesthetist to diagnose early or sudden bradycardia, or a disconnexion, seems somewhat illogical.

If these rules were followed to the limit then, on some of my operating lists, there would need to be at least two trained anaesthetists or half the patients. Most trained anaesthetists have surely developed enough experience to know when it is safe to go and insert a cannula into the next patient, look into the recovery room to see that all is well and perhaps even have a cup of coffee. Our recovery nurses would be upset and would probably resign if the anaesthetist always stayed until the patient was awake.

Physical presence in the theatre does not always guarantee safety. For instance, there is the famous case of the consultant and the senior registrar who were so busy talking together in the theatre that neither of them remembered to connect the patient to the ventilator; the patient survived his prostatectomy only because the dose of tubocurarine had not, fortunately, completely paralysed his respiratory muscles.

There are many areas where the anaesthetist, if not vigilant, can harm the patient. Who else, for instance, regularly administers so many drugs checked only by himself. Some of our operating department assistants and senior sisters are very capable and enjoy the occasional chance to look after the patient, but the responsibility still rests solely with the anaesthetist. At what stage is a junior senior house officer considered fit to mind the patient? Surely this is for the anaesthetist in charge to decide.

Let us not pick on just one aspect of anaesthetic practice, but look at our own practices as responsible anaesthetists and make sure that the charge of manslaughter does not fall on us. Perhaps Dr Green has information about anaesthetic malpractice which it would be useful for us all to hear about, so we can learn from it. If I were a member of the Medical Protection Society I should be somewhat concerned as to who the Society was protecting, doctor or patient, when he suggests a manslaughter charge in an Editorial in *Anaesthesia.*

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A reply

Dr Hepton seems to have misinterpreted the intention behind the Editorial. This was not an attempt to criticise the general standards of anaesthesia and monitoring, which the author believes to be of a high standard in the United Kingdom, but to draw attention to one aspect of anaesthetic practice, namely constant vigilance, which has caused concern to the defence societies, in view of the increasing incidence and costs of litigation. Of course, the possibility of a manslaughter charge is extremely unlikely, albeit that it has happened on occasion. However, it is salutary to note that, if the circumstances in which the anaesthetist leaves his anaesthetised patient suggest a serious lack of concern for that patient's welfare, the possibility of a serious criminal charge cannot be discounted. Even in a civil claim for damages, it can be very difficult to satisfy the court that it was necessary for the anaesthetist to delegate the care of his patient to an ODA when the accident occurred. In such circumstances, believe me, the anaesthetist would be given a very hard time.

The case quoted in Dr Hepton's letter is an example of the type of incident which constant vigilance would avoid and the objective of the Editorial.

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Labels for drug ampoules

Dr Guratsky correctly points out (*Anaesthesia* 1986; **41:** 337) that my earlier letter (*Anaesthesia*, 1985; **40:** 912–3) only touched briefly on the labelling of ampoules. This was because its theme was the need for clear standard labels for user-filled syringes. However, ASTM Subcommittee D10-34 spent 2 years evolving D4267, the standard specification for labels for Small Volume Parenteral Drug Containers. This standard requires that type size for the name of the drug, the amount of drug per unit (mg/ml) and the total volume be as large as possible (2.5 mm high or larger preferred). Good contrast is to be provided between the label text and either the drug container or an added opaque label background, so that the label is legible at 500 mm (arm's length) in a light of 215 lux (dim hospital corridor lighting) by a person with 6:6 unaided or corrected vision.

Manufacturers are encouraged to use acceptable abbreviations and to minimise non-essential copy. Adoption of this standard by manufacturers has led to a noticeable improvement in the legibility of labels on ampoules and vials.

A similar approach has been used to improve the ease of identification of pre-filled emergency drug syringes, the plastic barrels of which are unmarked. The drug names on the glass drug containers are poorly legible and disappear into the barrels as the contained air is expelled. The new proposed standard, requires that the drug's name in print, 5–8 mm high on an opaque background, can easily be read even through the plastic barrel at the distance of 155 cm (5 feet) in dim corridor lighting. This same standard also requires that drugs which must be diluted before administration, like potassium chloride, 10 or 20% lignocaine or dopamine, should preferably be supplied as a powder in a plastic squeezable container with a spike to facilitate addition of the powder to a container of parenteral solution. If supplied as a concentrated solution, the container shall not resemble a syringe and shall be unsuitable for direct intravenous line injection. The container also shall not allow the use of a standard syringe to transfer the concentrated solution to a container of parenteral solution.

Until these drugs are available as powder, or in the safer liquid containers, we recommend that such concentrated solutions should not be distributed around the hospital, but should be kept in the hospital's pharmacy whence they can be supplied suitably diluted, ready for use. These standards will be limited in application to the U.S. but we would be pleased to cooperate with other national committees to work towards international standards to solve these problems. Present national and international anaesthesia standards committees are fully occupied with standards covering the mechanical aspects of anaesthesia and ventilatory apparatus so additional volunteers will be needed to form new committees.

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Postoperative nausea and vomiting

The study by Dr Uppington and colleagues (*Anaesthesia* 1986; **41:** 16–20) draws attention to the very high incidence of postoperative vomiting that still exists. Most of this vomiting occurs in the ward rather than in the recovery area, so it is only when the anaesthetist visits the patient postoperatively, or requests a questionnaire to be completed, that the severity of the problem is fully appreciated.

We agree that there are many known factors that influence the incidence and severity of postoperative nausea and vomiting. In our own study of gynaecological patients undergoing laparoscopy, the incidence of vomiting was reduced from 49% to 17% ($p < 0.005$) when an anaesthetic technique which avoided the use of nitrous oxide was employed.[1]

There is increasing evidence of the side effects of nitrous oxide. The reduction in myocardial contractility in short term exposure to nitrous oxide[2] is likely to be clinically significant in some patients. Intermediate and long-term exposure causes inactivation of methylcobalamin producing leucopaenia and megaloblastic anaemia[3] with the possibility of reduced resistance to infection and impaired wound healing.[4]

Nitrous oxide is one of the oldest general anaesthetics in current use, but perhaps it is time to consider omission of this agent from routine anaesthesia.

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Air embolus and epidural anaesthesia

We read with interest the special article by Dr Crawford on maternal complications of epidural analgesia for labour (*Anaesthesia* 1985; **40:** 1219–25) and would like to comment on the inadvertent injection of local anaesthetic intravenously.

We have recently been in the habit of placing a Doppler ultrasound probe over the right atrium whilst performing the epidural, using the loss of resistance to air technique. This has revealed a high incidence of small amounts of intravascular air; in 35% of cases some air embolism was heard. Visible evidence of this vascular trauma was not always present, since blood was seen in the needle or aspirated down the catheter in only half of these cases. Perhaps these subclinical breaches of the epidural vessels may be reopened by trauma from the catheter, or high pressure following injection of the top-up dose of local anaesthetic.[1] This may explain the fact that two of the reactions described by Dr Crawford occurred only after several apparently uneventful top-ups.

This sensitive method of detecting air embolism[2] may also reveal air from other sources, particularly from the free running intravenous fluid load which may entrain small amounts of air. A previous publication on air embolism in epidurals[3] reported an incidence of 43% and warned about the dangers of paradoxical air embolism. The dangers associated with a patent foramen ovale must be extremely small in practical terms, as Dr Crawford does not mention this potential problem. However, the possibility of air embolus should be remembered when giving an epidural to anyone with congenital heart disease.

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A reply

Thank you for the opportunity of replying. The proposed safety measure might well be of considerable value during initiation of an epidural, when the hazards associated with an inadvertent intravenous injection should be most easily and rapidly contained, but I doubt that my midwives would take kindly to the suggestion that they should apply it preparatory to each top-up. Frankly, I would not dare to tender such advice!

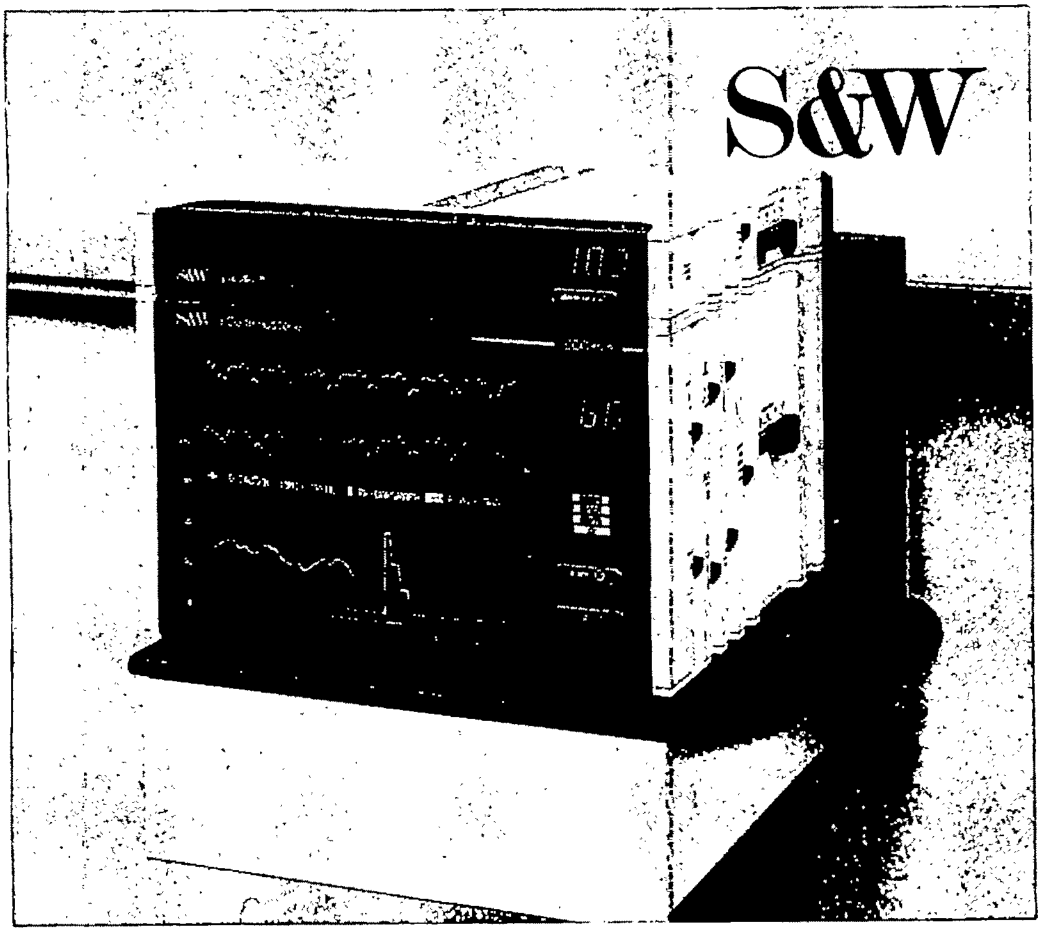
The Birmingham Maternity J.S. CRAWFORD
Hospital,
Birmingham B15 2TG

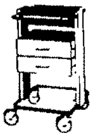
Time course of actions of combinations of muscle relaxant drugs

The paper of Pandit *et al.* (*Anaesthesia* 1986; **41:** 151–4) which reported a study of the time course of action of vecuronium and pancuronium mixtures, demonstrates that anaesthetists consider the use of relaxant combinations in order to modify the effect of one component of the combination.

We would like to report the hazard resulting from the use of gallamine triethiodide in combination with vecuronium since other anaesthetists might choose to use this agent to avoid potential bradycardia.

Bradycardia, associated with inadequate cardiac output, has occurred in four patients when vecuronium was used as the sole relaxant in a fentanyl, thiopentone, nitrous oxide, oxygen and halothane anaesthetic sequence, without anticholinergic premedication. We have subsequently used vecuronium and pancuronium mixtures in an attempt to avoid bradycardia but, like your authors, recognised that the use of pancuronium prolonged the period of muscle relaxation. We decided, in view of this, to use a vecu-

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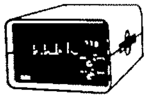
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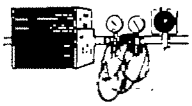
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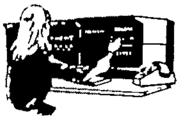
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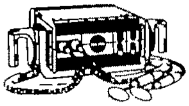
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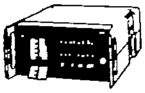
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BOOKS AND JOURNALS

24-28 Oval Road, London NW1 7DX, U.K. *Orlando, FL 32887, USA.*

ronium and gallamine triethiodide mixture, since gallamine has a shorter duration of action than pancuronium.

However, when a mixture of 0.6 mg/kg vecuronium and 1.0 mg/kg of gallamine was used in a fentanyl, thiopentone, nitrous oxide, oxygen and halothane sequence without anticholinergic premedication, we found that in two young patients (ASA grade 1) ventricular ectopics and bigeminy occurred at tracheal intubation and lasted for some 10 minutes. Ectopics recurred after atropine 1.2 mg and neostigmine 2.5 mg were administered to reverse muscle relaxation.

In an attempt to avoid this complication we reduced the dose of gallamine to 0.3 mg/kg with 0.1 mg/kg of vecuronium. This mixture was used satisfactorily in eleven patients but in the twelfth, use of atropine and neostigmine resulted in frequent ventricular ectopic beats which were controlled with intravenous lignocaine. This further dysrrhythmic episode suggests that any combination of gallamine with vecuronium may increase the risk of dysrrhythmias during anaesthesia. We have informed the manufacturers and the Committee on Safety of Medicines of our findings.

We would stress that in our view the use of vecuronium/gallamine mixtures is potentially hazardous and great caution be exercised if such a mixture is employed.

Lewisham Hospital,
London SE13 6LH

J.M. CUNDY
A. CRANSTON
M. ROSE

Anaesthesia and the public

Dr Green's thoughtful Editorial (*Anaesthesia* 1986; **41:** 129–30) on the safety aspects of anaesthesia underlines one of the most important implications of our work. We have to accept far more exacting standards than any other specialty, a situation which always puts us in a defensive position and is exemplified by the phrase 'death during general anaesthesia', with its accusatory medicolegal implications. Our physician colleagues are rarely held accountable for their failures and even with their increasing involvement in invasive procedures such as cardiac catheterisation or transluminal coronary angioplasty, a catastrophe or death is readily attributed to natural causes, recognised hazards or the ensuing emergency surgery! As for surgery and its multiplicity of minor and major complications, how often is the operator's competence questioned? On the other hand, a chipped tooth, sore throat, awareness, aches and pains, a haematoma, let alone grave complications, are widely regarded as a reflection on the anaesthetist and even an opportunity for lucrative litigation, despite the underlying problems they commonly reflect. Patients are often, and understandably, afraid of not waking up afterwards, but public ignorance about our work (including our high and exacting qualifications) is widely shared by colleagues in other branches of medicine. Does all this matter, except perhaps for our *amour propre?* Yes, it does. Our specialty must maintain a good image if it is to continue to attract today's galaxy of talent. Ultimately we can only protect our high standards if we have an informed profession and public and hence appropriate influence in powerful quarters on important matters. Let us be frank about another aspect; our work is also our livelihood and my impression is that our leaders have constantly to ensure that we are adequately rewarded (no more), both in the public and private sector. Previous battles have been fought, for example during the establishment of the first professional chair in anaesthesia and at the start of the National Health Service.

No doubt, our several specialty bodies regard the present customary processes of consultation as adequate. However, they have yet to dispel a widespread public view that we are merely technicians, or at best failed doctors, whose main task is to administer just an injection. Why, we the largest single specialty, do not even have our own College and are simply lodgers in the surgeons' dwelling place! We are still paying for the rag and bottle epoch when perhaps our specialty was indeed the last refuge of the inadequate medical practitioner, although the wheel long ago turned full circle and the anaesthetist is again a highly skilled physician. Maybe one day the Royal College of Anaesthetists will appoint a public relations (education?) officer. Naturally, we leave the eager search for baubles and the limelight to our colleagues in less retiring specialties, but an informed public is a worthwhile goal. At least it might reduce litigation!

20 Hocroft Avenue,
London NW2

A. GILSTON

Apparent postoperative recurarisation

We read with interest the letter from Dr Denny and colleagues (*Anaesthesia* 1986; **41:** 441) and would like to offer a possible explanation. They have demonstrated that during an infusion of atracurium, with a constant core temperature, but with a falling peripheral skin temperature, there is an observable decrease in the amplitude of the compound electromyographic action potential of the hypothenar muscles as measured by a Relaxograph.

It is well recognised by workers in the field of neuromuscular transmission that even during normothermic procedures it is vital to keep exposed limbs warm if they are being used for electromyographic (EMG) recordings and if the recording is to return to the control level. Indeed, on the trace published there is initially a clear increase in amplitude of both T_1 and T_4 as the peripheral temperature increases from 29–29.3°C, but the amplitude of these two responses decreases as the peripheral temperature falls and recovers again as the periphery rewarms. It would be interesting to know if the peripheral temperature was measured from the same hand as used for the EMG recordings.

We agree with the conclusion that there may be discrepancy between respiratory muscle function and observed neuromuscular transmission via the ulnar nerve but suggest that, on this occasion, this is a result of temperature-related changes in skin impedance rather than any specific effect on neuromuscular function.

University Department of Anaesthesia, M.A. Fox
Royal Liverpool Hospital, J.M. Hunter
PO Box 147,
Liverpool L69 3BX

A defective Tuohy needle

A false sign of loss of resistance to injection of air during an epidural injection was caused by a hole in the side of this disposable Tuohy needle (Steriseal) (Fig. 1). The needle had been inserted to a depth of 3 cm and initial depression of the glass plunger met with no resistance. Epidural catheters without holes have previously been reported,[1] but have needles with extra holes?

10210 Mantua Lane, A.J. Shribman
Richmond,
Virginia 23236, USA

Reference

1. Husemeyer RP. A defective epidural cannula. *Anaesthesia* 1980; **35:** 922.

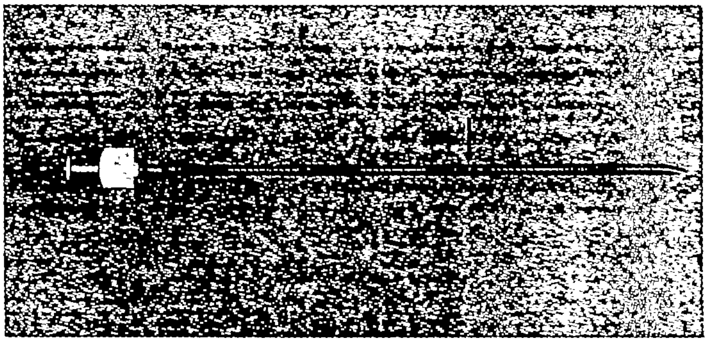
A reply

We have never before seen a needle with an extra hole over the last 25 years and during the production of millions of Tuohy needles. We assume that this fault arose during the manufacture, by welding, of the needle tube from a flat strip of stainless steel, but we have not been able to examine the needle.

This is indeed a very rare occurrence and one which would be extremely difficult to identify during the standard quality control procedures, which ensures a clear passage of air through the needle. Clearly, these procedures now require revising and we are doing so.

We very much regret the inconvenience caused and appreciate the understandable concern.

Needle Industries Ltd, A.M. Powell
Studley,
Warwickshire B80 7AS



Force exerted on epidural catheters

We read with interest the paper by Dr Hardy (*Anaesthesia* 1986; **41:** 306–8), and would like to comment on our recent findings.

We measured the force at which an epidural catheter (polyvinyl) will break if pulled through a fixed epidural needle. Three tensile loading tests were carried out:

straight forward loading, pulling the catheter through an axially aligned fixed needle and a catheter looped back on itself after passing through the fixed needle.

Loading tests on polyvinyl catheters showed that straight forward loading produced breaking loads of 20–25 N and that the catheter stretched to several times its original length. When the catheter was pulled through an axially aligned fixed needle, it showed thinning of the catheter as it stretched, but without contact with the cutting surface of the needle. When the catheter was looped back on itself after passing through a fixed needle, the cutting edge sliced through the catheter with a very little applied load (below 1 N).

An epidural catheter passed through a successfully placed epidural needle can be abnormally placed,[2] or may knot within the epidural space.[3] It is essential to re-emphasise that in the above situations both the epidural needle and the catheter should be removed simultaneously, because if the catheter is pulled out on its own, it may be sheared by the cutting edge of the needle or, if it has lodged abnormally, the catheter can stretch to a considerable length before breaking.

Queen Elizabeth Hospital,
Birmingham B15 B. KUMAR

Dudley Road Hospital,
Birmingham B18 F. MESSAHEL

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2. BROWNRIDGE P. Another misplaced epidural catheter. *Anaesthesia and Intensive Care* 1984; **12**: 369–71.

A reply

Thank you for the opportunity to see the letter by Dr Kumar and Dr Messahel. One hopes that they did not misinterpret my article which was concerned with the compressive force exerted *by* catheters, not *on* them. It would be interesting to correlate compressive forces and breaking forces for catheters of different materials and diameters.

Other factors influence the mechanical performance of epidural catheters. Belatti and colleagues[1] examined most of the available catheters and needles and the effects of these factors on catheter shear. The combination least liable to shear is a Portex nylon catheter with a Portex epidural needle! Another factor is the effect of temperature. In studies described elsewhere[2] a significant reduction in force was noted with a rise in temperature from 20–37°C for both nylon and polyethylene catheters. Epidural catheters show significant thermal transfer and rapidly equilibrate to the surrounding temperature.[3] This would presumably influence the performance of catheters to stretching and shearing forces.

Walton Hospital,
Rice Lane,
Liverpool L9 1AE P.A.J. HARDY

References

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2. HARDY PAJ. Epidural catheter tip rigidity (Unpublished).
3. WALMSLEY AJ, PONTE JC, WRIGHT D. Temperature changes along an epidural catheter: experimental and theoretical calculation. *British Journal of Anaesthesia* 1984; **56**: 803P.

Median epidural septum and multiple cannulation

Dr Nunn and Dr Mackinnon, in their description of a dual catheter technique for the management of unilateral epidural block (*Anaesthesia* 1986; **40**: 439), point out the lack of any previous reports of this method. This occurs in the same issue as an Editorial deploring the reluctance of anaesthetists to report problems in their practice (albeit specifically in drug use). Thus encouraged, this is a report of two cases which ultimately compelled me to use *three* epidural cannulae for successful control of pain in labour.

Patient 1

The concept of a dorsomedian septum in the epidural space was forcefully made in this primigravid patient of 25 years with a breech labour. An epidural block was initiated by a trainee with bupivacaine 0.5%, which resulted in good anaesthesia on the left side but no effect on the right. On being asked to advise in this situation, I carried out various standard adjustments, including withdrawing 1 cm of cannula, using supplementary 0.5% bupivacaine in the right lateral position and re-siting the epidural in an adjacent space. All this resulted in complete paresis of the left leg, but still no analgesia on the right. A sitting top-up for perineal pressure before full dilatation was effective bilaterally and provided suitable conditions for the subsequent delivery.

The same patient returned 18 months later in labour with a vertex presentation and requested another epidural for pain relief. On this occasion there was excellent analgesia on the right side with no effect on the left! This could not be improved despite supplementary 0.5% bupivacaine in the left lateral position. Full dilatation was reached before the cannula could be resited and she delivered spontaneously with marked bilateral perineal analgesia.

Patient 2

An epidural was requested in a 24-year-old patient, para 2, with a hydrocephalic baby, dead *in utero*, presenting by the breech. It was impressed upon me that the analgesia should be effective and reliable in this most distressing situation. The first cannulation provided excellent analgesia on the right, with no effect on the left, which could not be relieved with supplementary doses of bupivacaine. With the previous patient in mind, a second cannula was inserted into an adjacent space, without removing the first cannula, which would have been usual. By this means, good analgesia was obtained on the left. When a top-up was required for right-sided pain, a trial dose through the left cannula was ineffective. Once again a median septum was postulated to account for this.

The patient then experienced perineal pressure before full dilatation, but top-up doses given through both cannulae had no effect on the perineum. Mindful of the charge to provide reliable and effective analgesia, it was decided to insert a *third* cannula through the sacral hiatus to administer caudal epidural analgesia. These various cannulae provided suitable analgesia for the rest of the labour (which lasted 11 hours in all) and the breech extraction of a stillborn baby after drainage of the hydrocephalus.

All cannulae were recovered complete and there were no subsequent after effects. The patient was extremely grateful for the quality of analgesia achieved and the attention that she had received.

Doncaster Royal Infirmary,
Doncaster DN2 5LT
P.W. Bailey

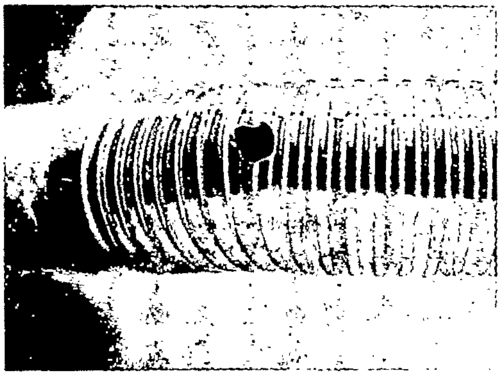
A silencer for high frequency positive pressure ventilation

A significant disadvantage for regular theatre work with the present-day generators of high frequency positive pressure ventilation is their noise output. This pulsating white noise, which is curiously hypnotic and which, on cessation leaves a dramatic stillness, can be reduced to a less obtrusive, more soporific sound by attaching a low resistance moisture and heat exchanging filter (Pall Ultipor Breathing System Filter, BB22-15) to the connector of the tracheal tube (e.g. Mallinckrodt Hi-lo Jet). It remains to be seen if such a filter will improve the warming and humidification capabilities of these devices, the paucity of which has bedevilled their development.

Freeman Hospital,
Newcastle upon Tyne NE7 7DN
I.D. Conacher

Unusual damage to a Bain system

A Bain system was checked prior to use and it was noted that the reservoir bag failed to fill despite closure of the expiratory valve with a 10 litres/minute gas flow. A hissing sound occurred and on close inspection a neat round hole was found approximately 5 cm from the proximal end of the outer coaxial tubing (Fig. 1). Further inspection and dismantling revealed another, similar sized hole on the inner tube (Fig. 2). Two small discs of material were found, corresponding to the outer and inner coaxial tubing holes. The inner metal delivery tube was noted to be deviated (Fig. 3), and the holes were related in position to the distal end of this



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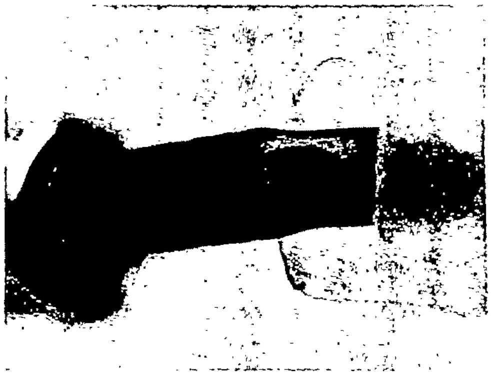

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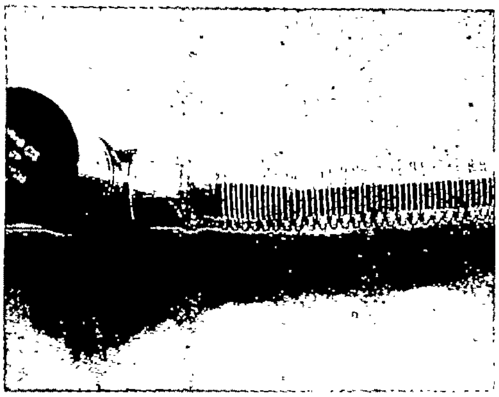

Fig. 3.

inner metal delivery tube, both in size and position. It was assumed the delivery tube had punched completely through both tubes.

The door between the anaesthetic room and theatre is just beside the wall-mounted Bain system in the anaesthetic room. Anyone rushing through the door from theatre to the anaesthetic room would have struck the system with the door very forcefully, leading to the deviation of the inner metal tube and puncturing of the circuit.

This damage to the Bain system was unusual in its degree and also in the fact that a leak occurred from the entire system as well as mixing of fresh and expired gas. The severity of the damage allowed easy detection on routine testing.

Presumably the incident was due to a violent knock from an anaesthetic room door, but the distal end of the inner metal tubing, as it is attached to the inner tubing, must have been too sharp. Furthermore, the anaesthetic system should not be mounted where it can be so easily damaged.

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A.J. HEWITT
W. CAMPBELL

Epidural meptazinol

We note with interest the letter from Dr Francis and Dr Lockhart (*Anaesthesia* 1986; **41:** 88) on epidural meptazinol following Caesarean section. We performed a study on the use of epidural meptazinol after Caesarean section, but a dose of 60 mg meptazinol was administered as the bupivacaine epidural began to wear off and the patient requested pain relief. The study was an open, prospective observational study in 10 patients. Standard exclusion criteria were applied and all patients gave informed consent.

Patient's pain severity was assessed before and after treatment using both visual analogue scores and verbal rating scores at 0, 5, 10, 15, 30, 45, 60, 90, 120 and 150 minutes. Baseline cardiovascular and respiratory parameters were also measured at these times. Statistical analysis using the Wilcoxon matched pairs signed rank test showed a significant degree of pain relief, which averaged 1.75 hours and varied between 1 hour and 2.5 hours. The only side effect reported was one patient who developed pruritus of moderate severity lasting for 2 hours. All 10 patients were eventually withdrawn from the trial because they required additional pain relief. No further side effects were noted in any patient. From our small study we would agree with Dr Francis and Dr Lockhart that the use of epidural meptazinol should be discouraged, but more because of the short duration of its action than because of the incidence of serious side effects.

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Leavygreave Road,
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R.J.S. BIRKS
D.R.G. MARSH

Location for delivery in a patient with Eisenmenger's syndrome

The obstetric and anaesthetic management of patients with Eisenmenger's syndrome remains a subject for debate in the literature. The problems, which include changes in systemic vascular resistance and shunt reversal, paradoxical air embolism, risks of fluid overload, thrombosis associated with polycythaemia, haemorrhage related to heparin administration and the hazards of intensive monitoring have all been discussed.[1,2]

Opinions vary about the current mode of delivery; elective section under general anaesthesia or epidural and vaginal delivery with epidural have both been successfully employed,[3,4] but most authorities agree that a team approach to management should prevail. One question which has yet to be decided is the location where delivery, if it follows labour, should be conducted in patients with this form of noncorrectable heart disease.

A 28-year-old Indian woman with an established diagnosis of Eisenmenger's syndrome had a forceps delivery at 34 weeks gestation. Labour was induced since the cervix was thought to be ripe and epidural analgesia was provided initially with 0.25% bupivacaine to a total of 8 ml. This was increased to 8 ml of 0.375% bupivacaine as the intensity of contractions increased. A total of three doses was administered.

Electrocardiograph, and blood pressure with an indwelling left radial artery line, urine output and the general condition of the mother were continuously monitored.

A live female infant with an Apgar score of 8 at 1 minute, and 10 at 5 minutes, was delivered with the use of forceps to prevent the possible adverse effects of pushing during the second stage 6 hours after induction of labour. The labour, delivery and immediate post delivery care were conducted in a cubicle in the intensive care ward. It was considered that the obstetric part of the management of the patient was not as potentially hazardous as her cardiovascular status and if further intervention were to be required, for example central venous or pulmonary artery pressure monitoring, infusion of vasoactive drugs or resuscitation, then the intensive therapy unit was the safest place for this. A midwife was brought from the labour ward to attend the mother and the usual ITU nurse was present to supervise monitoring of the cardiovascular and general status.

Obviously, the ideal solution to problems such as these would be an ITU-style room on the labour ward to which high risk women could be assigned and in which staffing with appropriate expertise can be guaranteed. Until this happy solution is widespread, the ITU may be the safest place for the high risk parturient.

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P.N. Robinson
K.G.A. Macleod

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3. Spinnato JA, Kraynack BJ, Cooper MW. Eisenmenger's syndrome in pregnancy: epidural anesthesia for elective Cesarian section. *The New England Journal of Medicine* 1981; **304:** 1215–7.
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Inhalation of mini-trach

We had a similar experience to Dr Leach (*Anaesthesia* 1986; **41:** 338) but thanks to the foresight of the nursing staff who stitched a piece of 1 cm cotton tape to one of the flanges the situation was controlled. The problem in this patient was that the loose skin at the front of the neck prevented adequate distraction of the flanges of the mini-trach tube and movement of the neck eventually caused the stitches to cut out.

We suggest that the risk of inhalation of these useful tubes could be avoided by the use of tape and suggest that this be incorporated into the design of these tubes.

Royal Cornwall Hospital,
Treliske, Truro,
Cornwall

R. Winter
G. Morgan

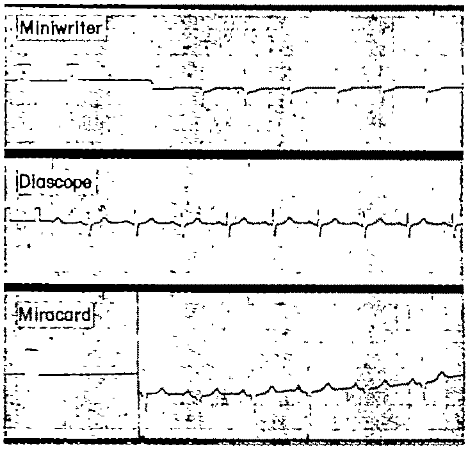
(*Editor: a flange for this purpose has now been incorporated by the manufacturers*).

ECG traces—a note of caution

The other day out of curiosity I recorded three traces on three different recording electrocardiogram machines from the same CM5 chest leads attached to one single patient. He was a fit, healthy man having a general anaesthetic and breathing spontaneously through a mask. The blood pressure and pulse rate were normal and stable. Three different traces from each of the machines were recorded (Fig. 1).

The equipment was kindly inspected by the District Electromechanical Equipment (EME) unit in their workshop. They found the following.

Miniwriter. The device might have been dropped or knocked quite severely. The permanent magnet to the galvanometer (stylus motor) had been moved from its original position, thereby causing nonlinearity of the stylus swing. The stylus pressure was so great that the chart speed was drastically affected.



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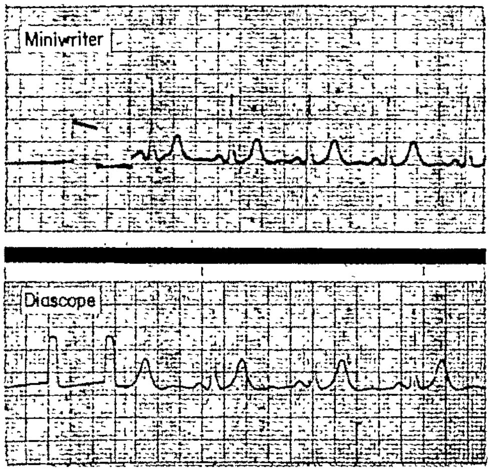

Fig. 2.

Diascope 2. The recording paper roll had been wrongly installed and the stylus contact was thus incorrect. The trace was therefore wider than it should have been. Because of the different point of contact the shape of the trace would be distorted to a greater or lesser degree. The drag imposed on the paper feed mechanism and motor would cause the chart speed to become erratic, introducing further distortion to the trace.

The faults were rectified by the EME unit and the equipment was used again on another patient to obtain two different traces. These results are shown in Fig. 2. This illustrates the need for regular functional checks on ECG equipment to establish correct operation.

The Queen Victoria Hospital,
East Grinstead,
West Sussex

H. PATEL

Induction of anaesthesia in children

This is to support Dr Carter's call for a more humanitarian approach to induction of anaesthesia in children (*Anaesthesia* 1986; **41:** 440). Adequate sedative premedication should indeed be the prime aim in paediatric practice, and physical restraint must play no part in the management of the struggling child. However, I would suggest that postponement of surgery until more substantial premedication has been administered is also not without its emotional trauma and should be avoided if at all possible. Following failed venepuncture, if gaseous induction cannot be accomplished with ease, immediate recourse to intramuscular ketamine (7 mg/kg) will rapidly produce narcosis even in the most uncooperative child.

May I also take this opportunity of appealing for a more liberal attitude towards allowing a parent to accompany children to the anaesthetic room. Surely, any anaesthetist who does not feel able to allow a parent to witness his technique, should not be performing paediatric anaesthesia unsupervised?

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R.H. JAGO

Anaesthesia, 1986, Volume 41, pages 886–887

Book reviews

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A Practice of Anesthesia for Infants and Children

Edited by J.F. RYAN, I.D. TODRES, C.J. COTÉ, N. GOUDSOUZIAN. Pp. 314. Grune and Stratton Inc., 1986. £56.00.

The editors of this volume are members of the anaesthetic staff of the Massachusetts General Hospital and are well known for their substantial contributions to paediatric anaesthesia and intensive care. The contents are based on the extensive experience of the Pediatric Anesthesia Group of this famous institution.

This is a most pleasing and readable book. Its 24 chapters provide comprehensive coverage of the subject and are of a uniformly high standard of content and presentation. The opening chapter defines the basic requirements for safe anaesthetic management of the child. While stressing the fundamental need for direct patient observation, the emphasis laid on measurements of respired oxygen and carbon dioxide concentrations, and on pulse oximetry, reflects the importance which is justifiably attached to patient monitoring in North America. There is an excellent and admirably illustrated section on the paediatric airway, although it would have been improved if topics such as subglottic stenosis and epiglottitis had been included here instead of being dealt with in less appropriate parts of the book. The account of the complexities of paediatric clinical pharmacokinetics is of considerable value. A chapter on 'neonatal emergencies' includes useful descriptions of tracheo-oesophageal fistula, diaphragmatic hernia and other respiratory and gastrointestinal disorders. However, there is rather undue emphasis on the medical and surgical aspects at the expense of more detailed anaesthetic management. Not all would advocate rapid sequence induction, which presumably means thiopentone and suxamethonium, in a newborn infant, even though there is no airway abnormality, nor would many prefer to use narcotics rather than inhalational agents in infants with pyloric stenosis.

There is a good chapter on the use of muscle relaxants in children by a recognised authority and, as would be expected, this is a well written and lucid contribution. A minor criticism is the rather lengthy discussion of neuromuscular monitoring and the lack of reference to the choice of these drugs in various diseased states. There is a most useful account of the fundamentals of paediatric neuro-anaesthesia. The chapters on cardiovascular physiology and pharmacology and on anaesthesia for children with heart disease are extremely comprehensive, a laudable feat considering the limited space available. A useful classification of heart disease based not only on cyanotic and acyanotic groupings, but also taking into account the haemodynamic effects of previous palliative and corrective surgery, is also included. The concluding two chapters of the book contain a wealth of practical detail relating to equipment and procedures such as venous and arterial cannulation.

Most of the chapters have an extensive and up-to-date list of appropriate references and it is perhaps understandable that the vast majority are of transatlantic origin. The volume is most attractively produced, on good quality paper with large page size and double column format, although the print is rather small. Its layout permits the inclusion of an unusually large number of high quality line diagrams and half-tone prints which greatly enhance its appeal.

It is the editors' wish that this book should fulfil the need for a text which is intermediate between the didactic and the encyclopaedic and there is every reason to believe that they have accomplished this aim. Practical manuals and extensive reviews of paediatric anaesthesia are already available and this volume should be used to complement rather than replace them. There is little to criticise in this eminently attractive and informative book. The editors, indeed all the contributors, are to be congratulated for producing a conveniently sized volume containing most of the information required for safe paediatric anaesthesia. It can be thoroughly recommended for the bookshelf of all with an interest in the anaesthetic management of children.

G.W. BLACK

Current topics in anaesthesia—Neonatal anaesthesia and perioperative care, 2nd edition

D.J. Hatch and E. Sumner. Pp. 268. Edward Arnold, 1986. Price: £33.00.

The title of the second edition of this monograph, No. 5 in the series Current Topics in Anaesthesia, has been expanded and now includes peri-operative care. The authors state that this is justified by the inclusion of material which is considered to make the book more attractive to non-anaesthetists. This objective may or may not be realised as the text remains essentially orientated towards the anaesthetic management of neonates.

The format of the book remains the same, but the text has been extensively revised and updated, with some reorganisation. Several concise sections have been added on such topics as immunology, the preterm infant and intensive care for cerebral protection. The number of unusual medical conditions and syndromes, which may tax both the neonatal anaesthetist's skill and his memory, have been increased in Appendix 1. The guidelines for drug dosage, Appendix 2, now include the newer neuromuscular blocking agents, antibiotics, inotropic agents and drugs for use in cardiopulmonary resuscitation. Several new figures and tables have been added and the lists of references and suggested further reading cite many publications dating from 1981 and originating from both sides of the Atlantic.

The basic principles of pre-operative evaluation, anaesthetic management and postoperative care of neonates are comprehensively covered, well reasoned and cannot be faulted. This edition has been expanded by some 60 pages, new information is presented and the authors have maintained the high standard of their previous edition. There are some minor criticisms, however, which do not diminish the overall value and appeal of the book. The techniques described understandably reflect the authors' preferences and wide experience at Great Ormond Street and many experienced neonatal anaesthetists may hold differing opinions on some of the practical aspects. Some would maintain that the establishment of reliable intravenous access is mandatory before intubation or induction of anaesthesia. The chapter on resuscitation is rather disappointing and it is unfortunate that the opportunity has not been taken to increase the relevance of this section by presenting an account of resuscitation in the neonatal period generally. The guideline dosage for a postoperative fentanyl infusion does not indicate its restriction to patients who are receiving controlled ventilation of their lungs.

All anaesthetists involved with the management of the neonate will benefit from reading this comprehensive and authoritative book, although the examination candidate, quite rightly, will find some sections too detailed. Paediatricians and surgeons, particularly those in training, should peruse at least the chapters on perinatal physiology, the surgical neonate and postoperative care. This edition should, therefore, be readily available in every hospital treating neonates. Unfortunately, the price, which has more than doubled since the first 1981 edition, may be a deterrent. Anaesthetic departments and hospital libraries, even those possessing the first edition, should seriously consider investing in the second. Aspiring and established paediatric anaesthetists should have their own copy.

P. Morris

Anaesthesia, 1986, Volume 41, pages 888–895

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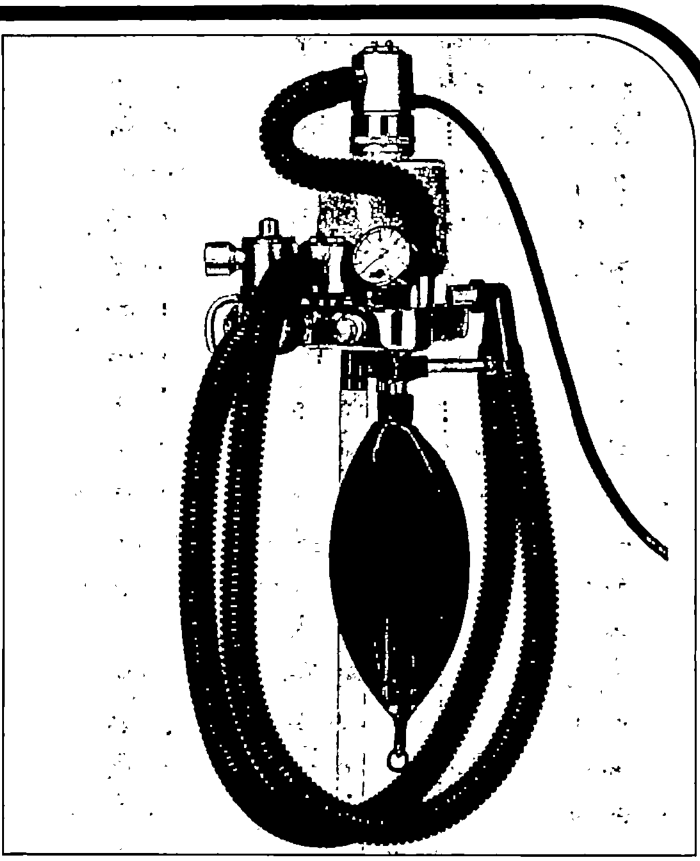

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Safety Information Bulletin

These are issued by the Department of Health and Social Security

Treonic C30 Infusion Controller

These have been supplied in the past by Vickers Medical but are now marketed by Travenol Laboratories Limited. There are three particular problems associated with their use.

1. It is important that the drop chamber be not tilted.
2. Some controllers do not establish and maintain control at infrequent drop rates, particularly below 9 drops/min.
3. The clamp mechanism within the controller does not always completely close the tube.

The latter two points require that the apparatus should be checked and if necessary the supplier of the particular C30 should be contacted.

Lung ventilator, Blease Manley Model MP3

The piston and seals of the expiratory tap assembly should be replaced annually. The plastic piston within this gradually becomes brittle with time and with regular autoclaving.

Syringe pumps: Vickers Treonic IP4 and IP5 series

A splashproof cover should be fitted to the flow selector switch of these models. Pumps with serial numbers greater than 118-002497 have also a switch-monitoring circuit. Models with lower serial numbers can be modified.

Enquiries about all the above may be made to the appropriate person as specified below.

England
Mr R.A. Page,
DHSS,
Scientific and
Technical Branch,
14 Russell Square,
London WC1B 5EP
(Tel. 01 636 6811 Ext. 3259

Wales
Dr J.A.V. Pritchard,
Scientific Adviser,
Welsh Office,
Cathays Park,
Cardiff CF1 3NQ
(Tel. 0222 823912)

Scotland
Scottish Health Service,
CSA, Supplies division,
Scientific and
Technical Branch,
Trinity Park House,
South Trinity Road,
Edinburgh EH5 3SH
(Tel. 031 552 6255
Ext. 2478)

N. Ireland
Chief Engineer's Branch,
Department of Health
and Social Services,
Central Works Unit,
Stoney Road,
Dundonald,
Belfast BT16 0US
Tel. Dundonald 4535
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The Institution of Mechanical Engineers

Engineering in Medicine Group/Engineering Sciences Division.
Seminar: Safety aspects of anaesthetic equipment.
2 October, 1986, The Institution of Mechanical Engineers, 1 Birdcage Walk, Westminster, SW16 9JJ
Information: Penny Whitehead (01 222 7899 ext. 213).

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........................19

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Association of Anaesthetists of Great Britain and Ireland

I (full name).. offer my name as a candidate
BLOCK LETTERS

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Qualifications (with dates)..

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(NAME IN BLOCK LETTERS)
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Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

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ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

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Volume 41 Number 9 September 1986

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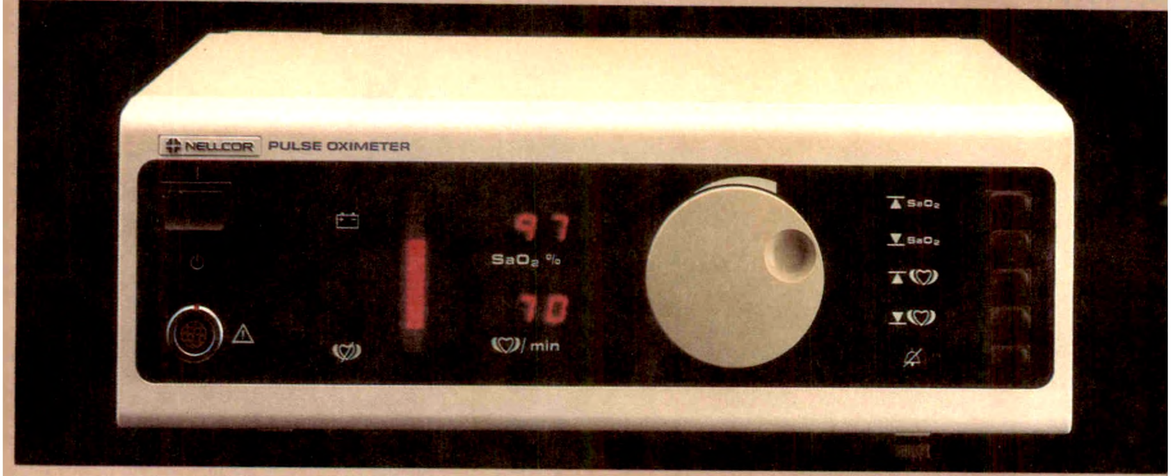

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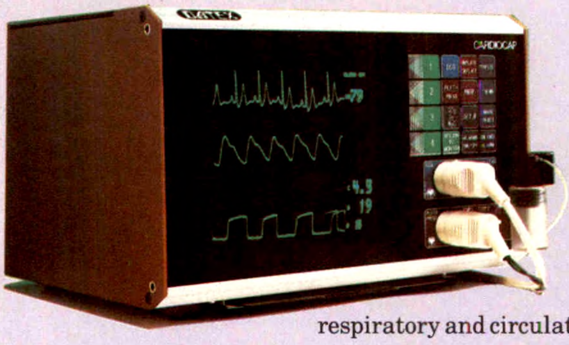

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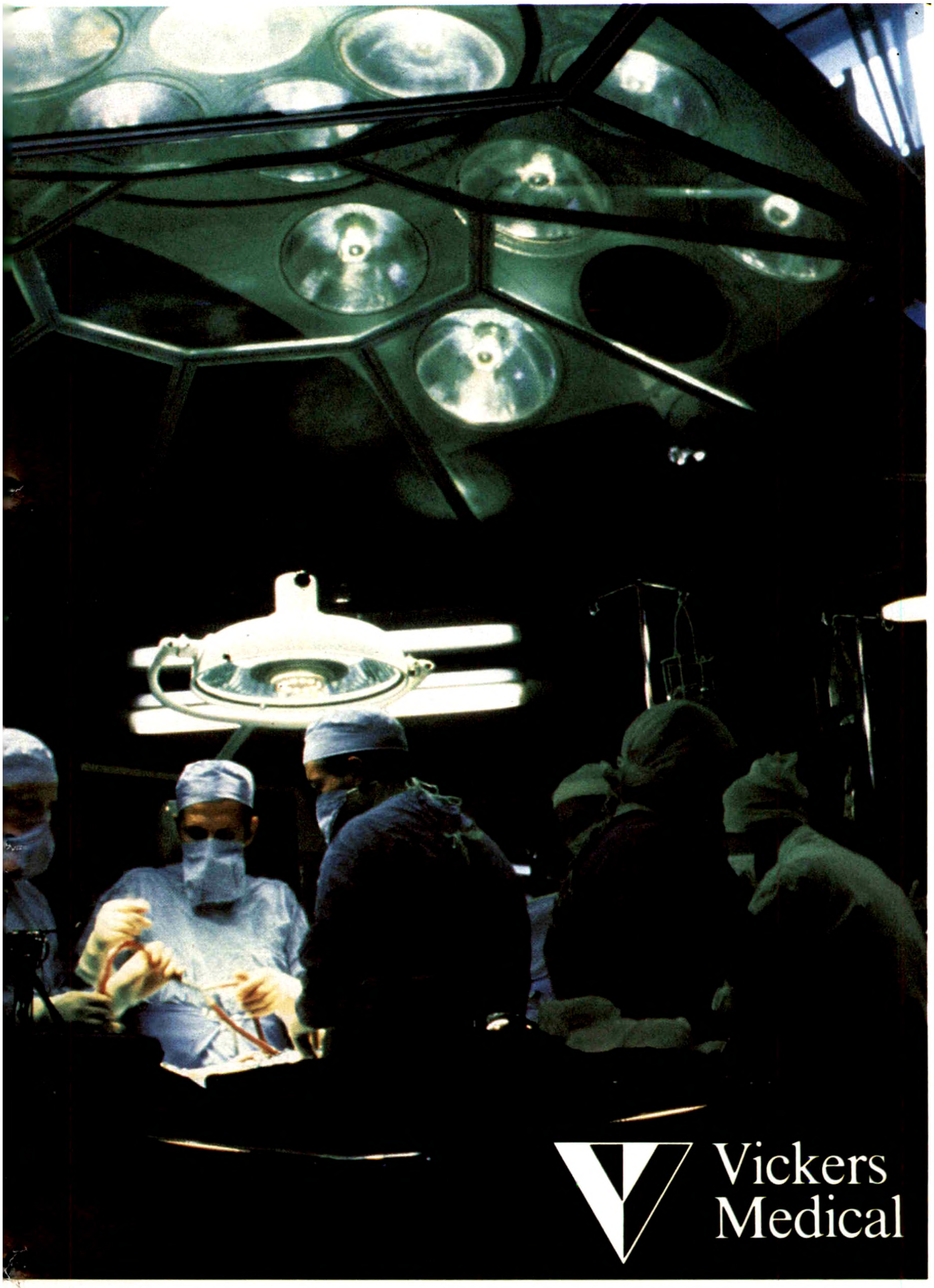

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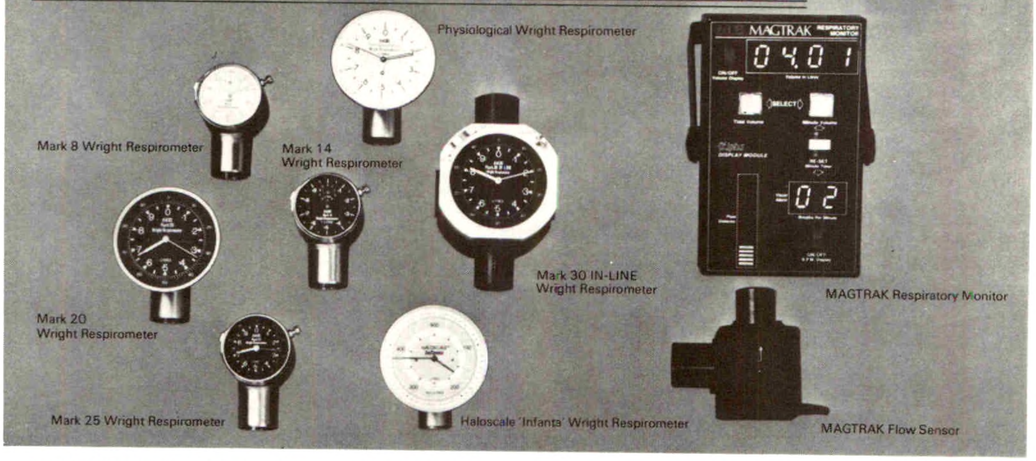
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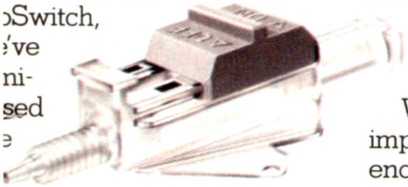

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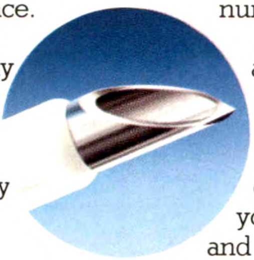

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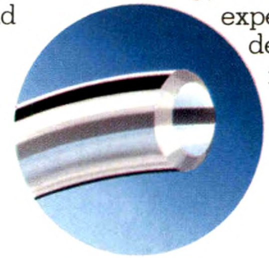

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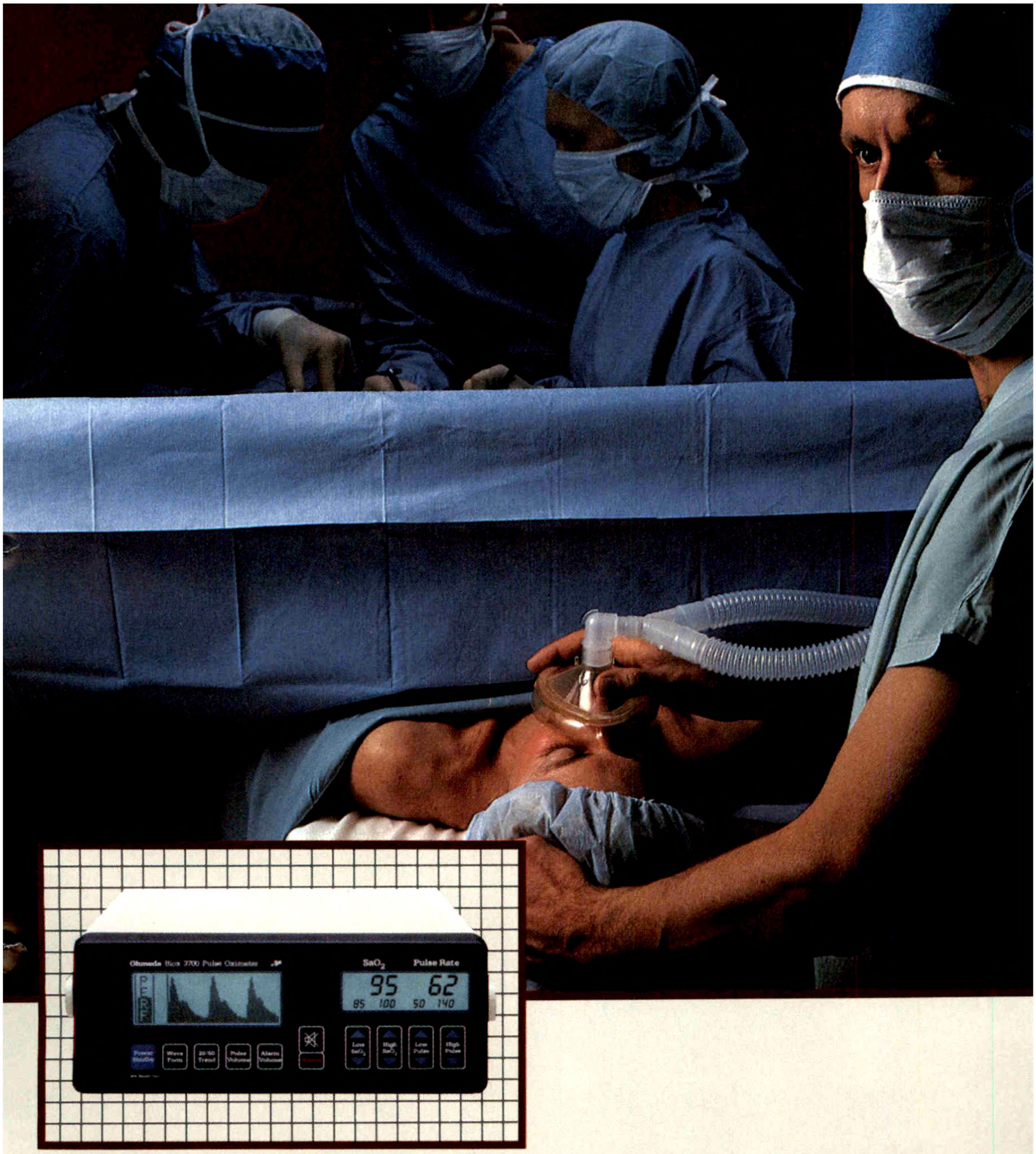

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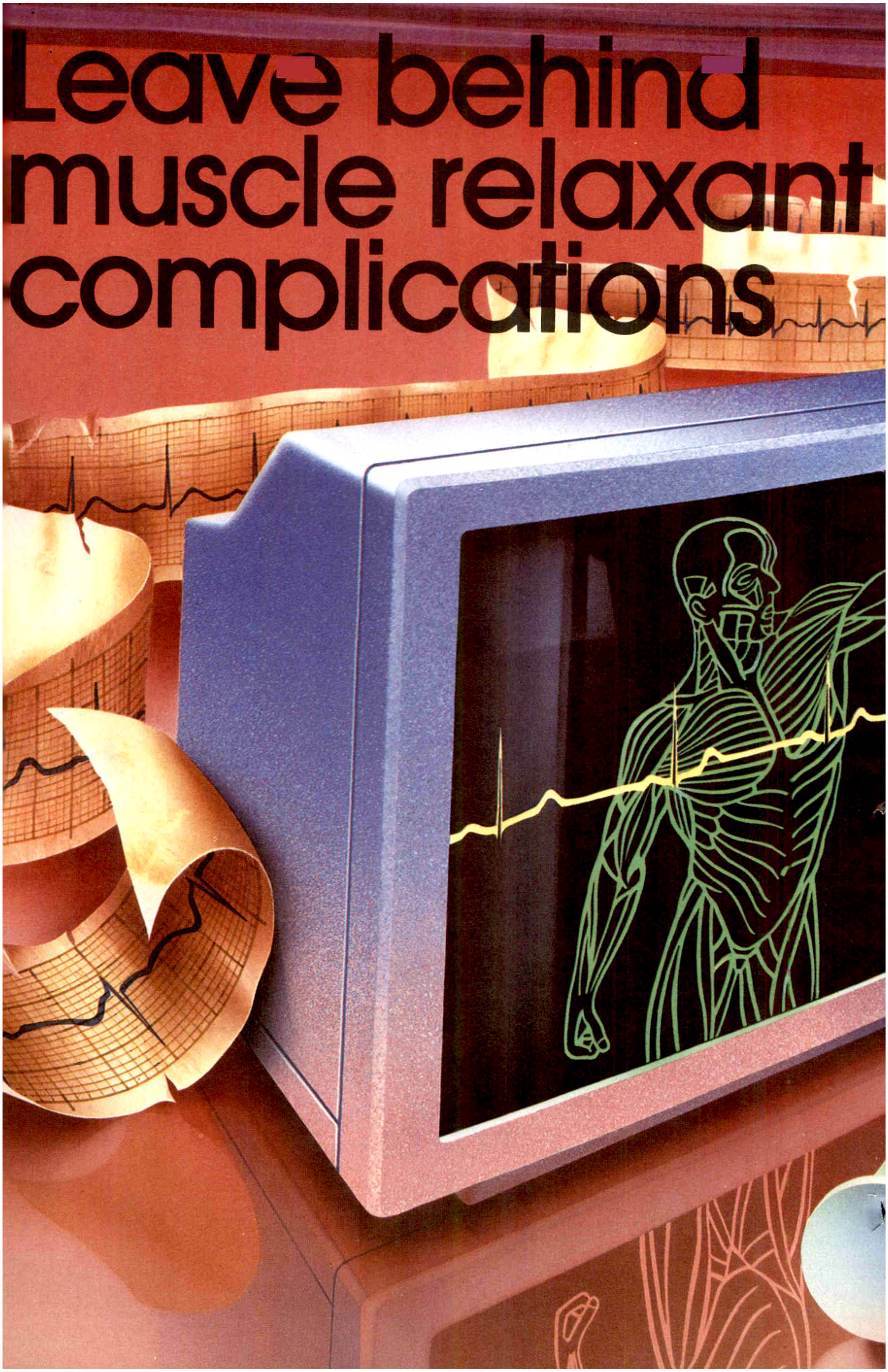
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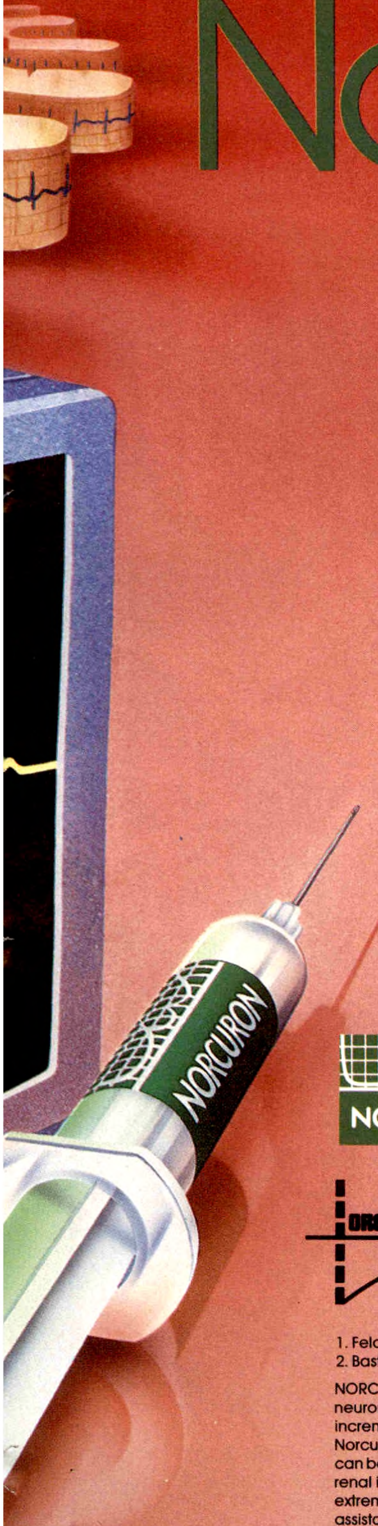

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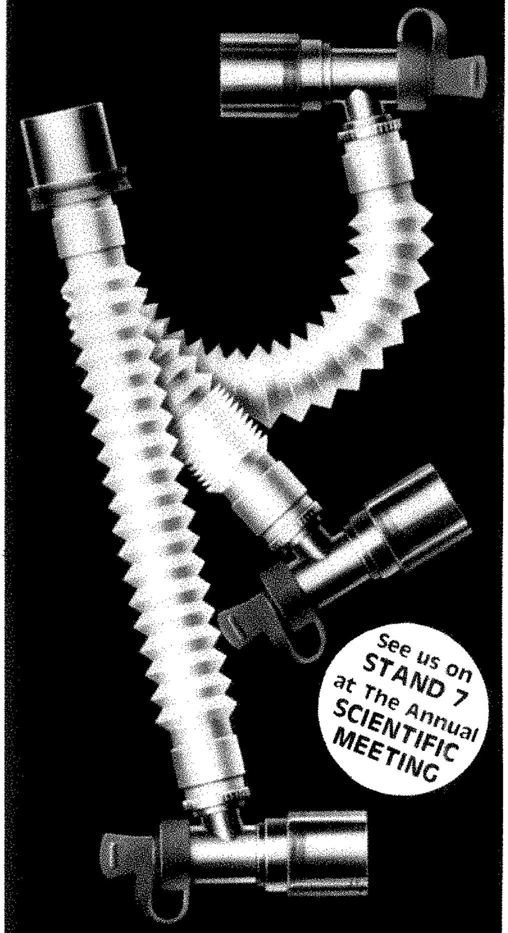

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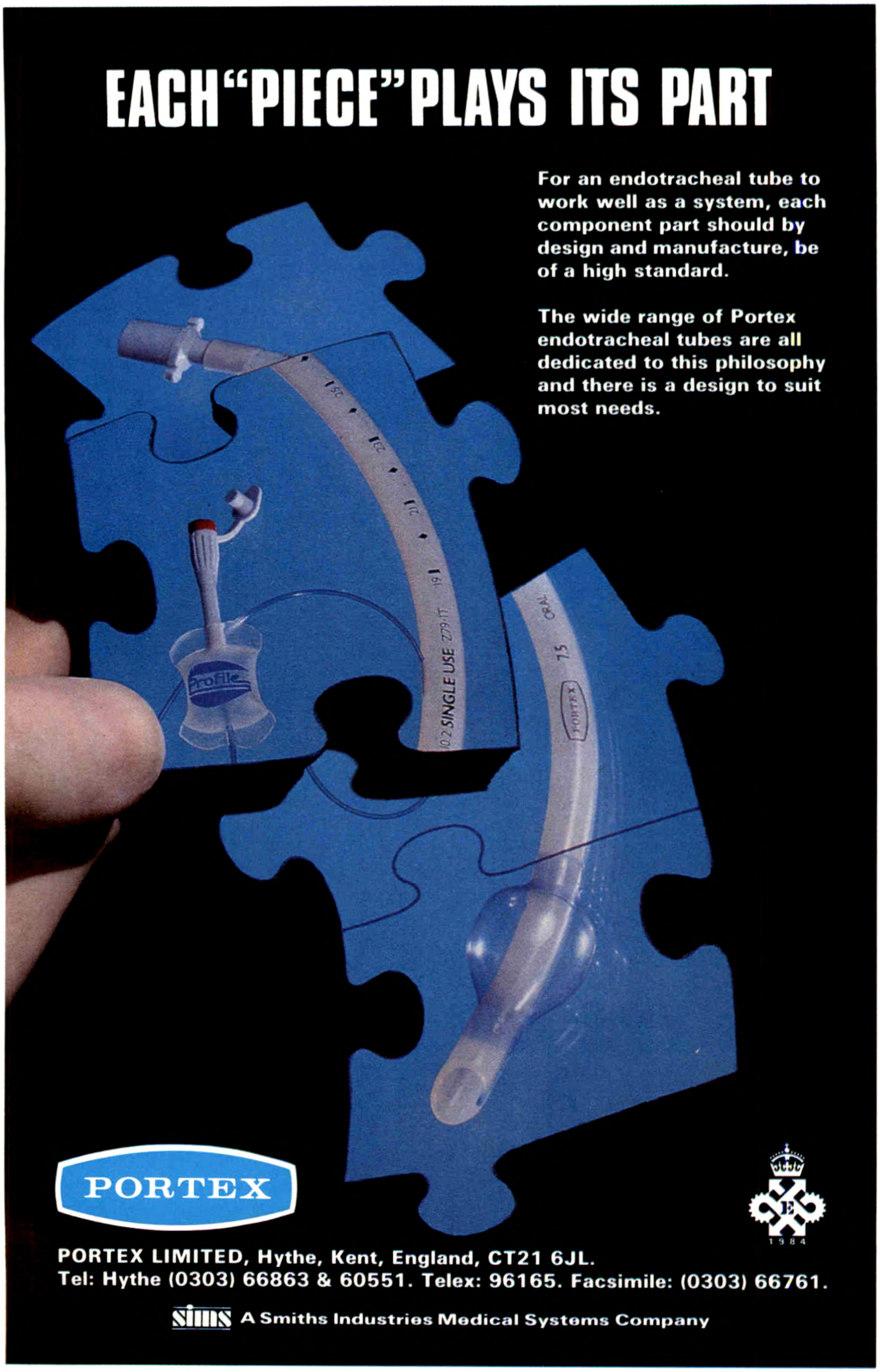

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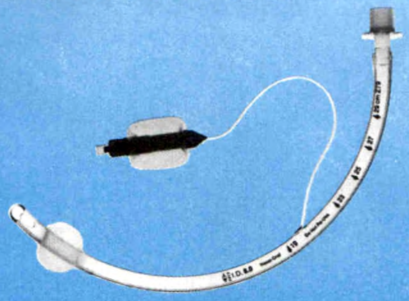

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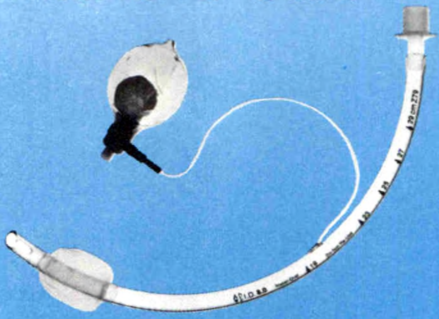

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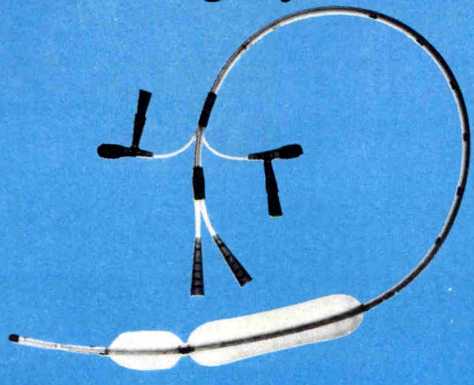

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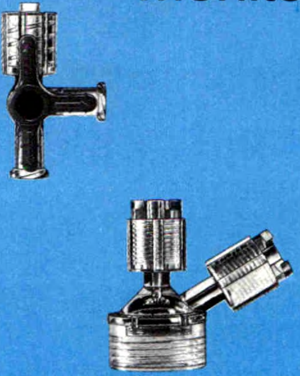

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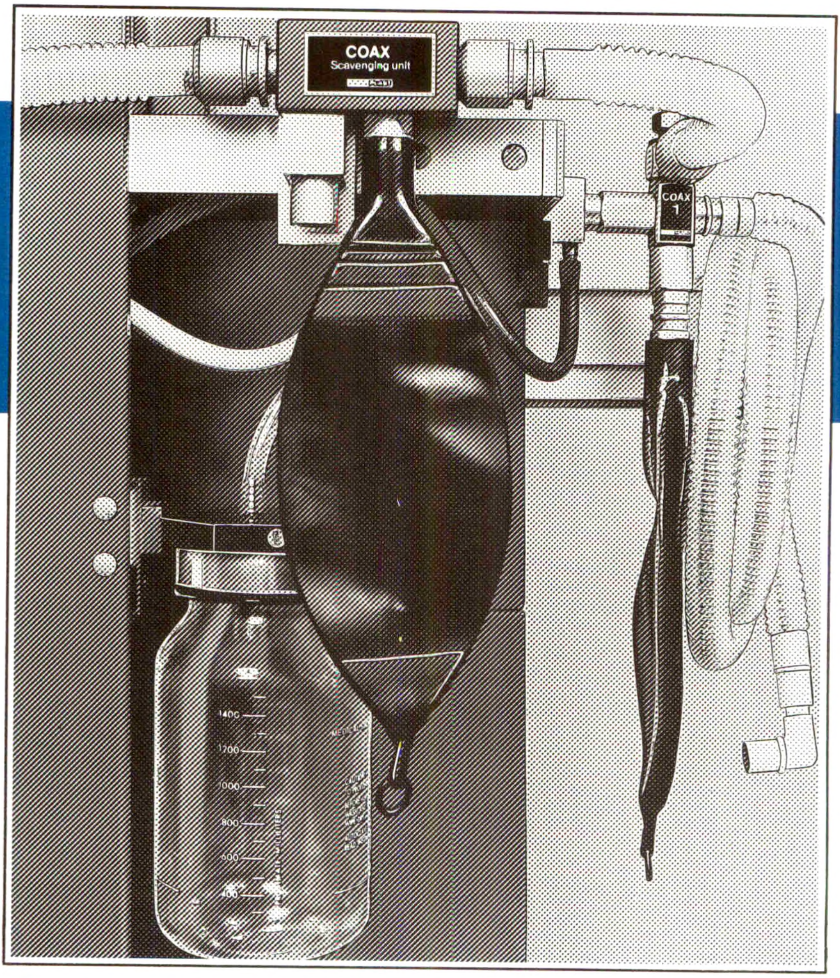

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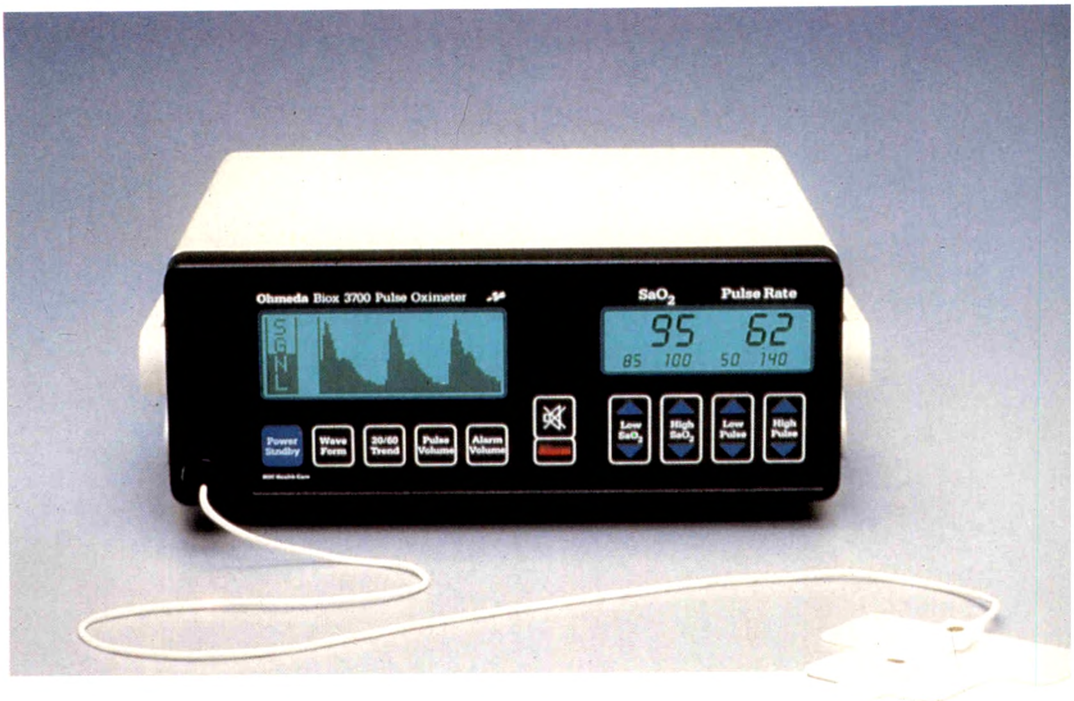

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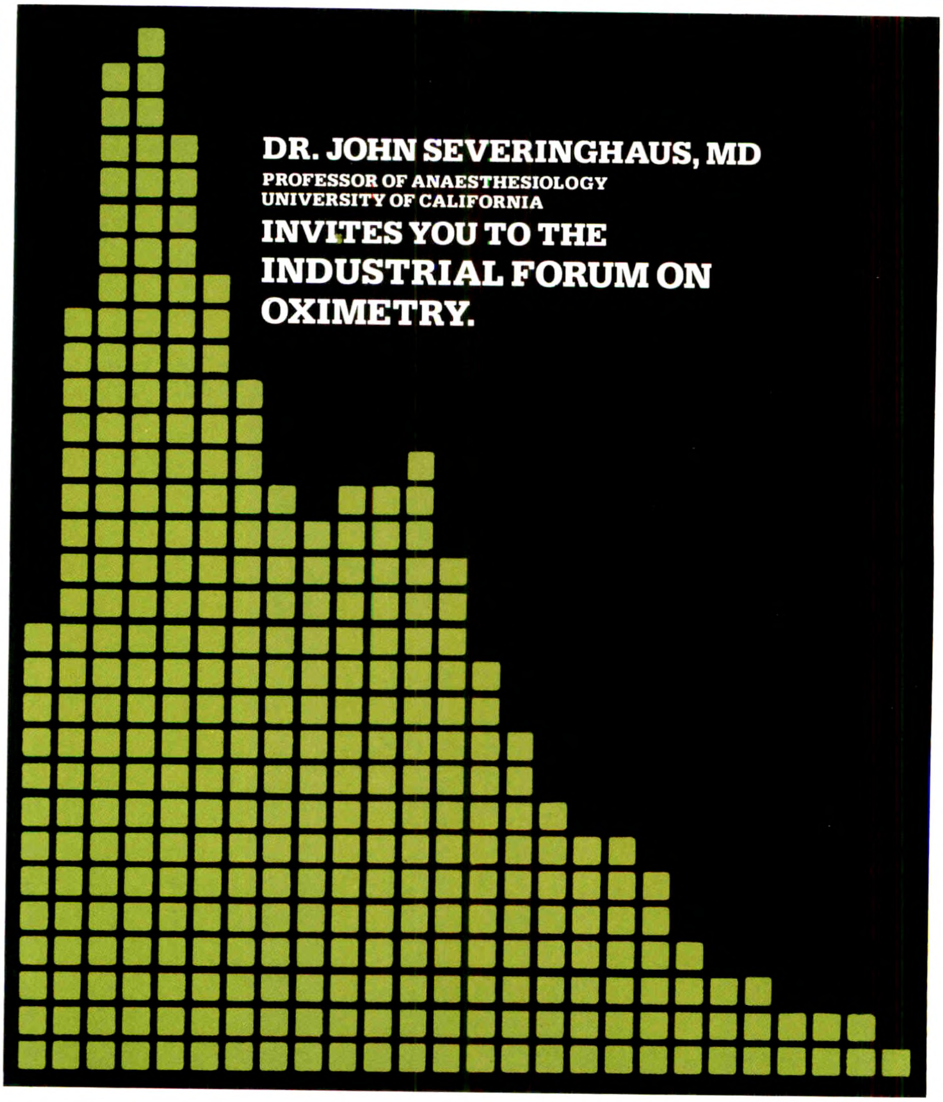

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Anaesthesia, 1986, Volume 41, pages 897–899

Editorial

Nitrous oxide during pregnancy

Physicians are often faced with the dilemma of whether they should extrapolate data from animal experiments or from only remotely related clinical reports to problems in their practice. The decision is made more difficult when directly relevant clinical studies either have not been performed or are inconclusive. Such a situation currently confronts the anaesthetist. There is incontrovertible evidence that nitrous oxide adversely effects vitamin B_{12} and folate metabolism. Because of this the recommendation has been made that the agent should not be administered to pregnant women in the first two trimesters of pregnancy.[1] Is this recommendation justified?

The first observation regarding the biochemical effects of nitrous oxide was made in 1968, when it was shown that nitrous oxide irreversibly oxidised vitamin B_{12} cob(I)alamin to cob(II)alamin *in vitro*.[2] Soon thereafter it was established that a similar reaction occurred in rats *in vivo* and that, as a consequence, methionine synthase (which requires vitamin B_{12} in the fully reduced state) was inactivated.[3] Methionine synthase activity is required for the conversion of homocysteine to methionine and for the demethylation of methyltetrahydrofolate. The latter is one of the precursors of 5,10-methylenetetrahydrofolate, which is required for the conversion of deoxyuridine (dU) to thymidine, a DNA base.

Inhibition of methionine synthase activity has been detected in liver biopsy specimens obtained from surgical patients after exposure to 50–70% nitrous oxide for 1.25–2.75 hours.[4] Abnormalities in vitamin B_{12} or folate-dependent DNA biosynthesis are measured with the dU suppression test which was employed by O'Sullivan *et al.*[5] to assess the effects of nitrous oxide on bone marrow function in surgical patients. In their study, bone marrow function was normal in 30 patients administered 50% nitrous oxide for up to 6 hours for routine surgical procedures. Other patients who received 50% nitrous oxide for 12 or for 24 hours had abnormal dU suppression values, but these had returned to pre-operative values when measured 12 hours after nitrous oxide was discontinued. Folinic acid, administered 12 hours and then again one hour before the 24-hour exposure to nitrous oxide, prevented abnormalities in the dU suppression test. Another study[6] showed that patients ventilated with 50% nitrous oxide for 24 hours developed megablastic changes in bone marrow.

Thus, one can conclude that methionine synthase inhibition occurs soon after nitrous oxide is administered to surgical patients. However, this is not translated into measurable effect on DNA synthesis, at least in bone marrow, unless exposure continues for 6–12 hours; these effects appear to be readily reversible. Not germane to the present discussion of acute exposure to nitrous oxide, is the fact that neurological symptoms resembling those seen in pernicious anaemia may develop as a consequence of many weeks or months of exposure to high concentrations of nitrous oxide. This is a problem restricted almost exclusively to abusers of nitrous oxide.

The above discussion is background to the questions raised by Crawford and Lewis in their article in this issue (p. 900). They examined hospital records for the years 1968–1984 of all patients who had an operation with nitrous oxide ($n = 463$) during the first two trimesters of pregnancy at two Birmingham hospitals. They compared this group with all pregnant patients who had similar procedures with regional anaesthesia ($n = 114$) during the same period from these two hospitals. The outcomes they examined were abortion, congenital malformation and low infant birth weight. Analysis of their data is somewhat complicated because the authors appear to consider the first trimester of pregnancy to have 16 weeks (the usual duration of a human trimester is 13 weeks). However, this does not alter their results; clearly, there were no differences between the two groups. Even if one were to disagree with the interpretation of some of the outcomes, such as those they attribute to 'personal communication with perinatal pathologists', it would be difficult to quarrel with their overall conclusions, that is, that

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Table 1. Blood gas, blood cyanide and gold levels

			<--- Bolus injections of $NaHCO_3$; in total 600 mmol --->					
Parameters	<----------------- 60% inspired O_2 ----------------->						<-- 100% O_2 -->	
Time (hours)	21.35*	22.05	23.50	01.00	02.30	02.40	03.10	05.15
pH		7.30		7.30	7.15		7.20	7.18
$Paco_2$ (kPa)		4.70		3.80	3.70		5.40	6.60
HCO_3^- (mmol/litre)		18.00		13.40	9.80		16.20	19.10
BE (mmol/litre)		−6.70		−11.20	−17.00		−10.50	−8.70
Pao_2 (kPa)		47.00		9.40	8.00		7.70	4.10
Plasma HCN (μmol/litre)	2.1		0.5			0.14		
RBC HCN (μmol/litre)	188.5		42.9			5.50		
Plasma SCN^- (μmol/litre)	91		95			101		
Plasma Au (mg/litre)			0.85					
RBC Au (mg/litre)			14.20					
Urine HCN (nmol in 30 ml)					21.00			
Urine SCN (μmol in 30 ml)					33.00			
Urine Au (mg in 30 ml)					0.50			

HCN, hydrogen cyanide; Au, gold; SCN, thiocyanate.
*300 mg cobalt edetate given after this blood sample was taken.

analysis initially showed good pulmonary gas exchange and a metabolic acidosis with respiratory compensation (Table 1). Later she became progressively more hypoxic, hypercapnoeic and acidotic.

Despite conventional treatment for anaphylaxis with adrenaline, steroids and antihistamines, and intensive supportive therapy with optimisation of circulating volume, high inspired oxygen concentration and massive infusion of sodium bicarbonate (600 mmol in total) her condition deteriorated, although she remained fully conscious until intubated at 02.05 hours. Ventilation of the lungs with 100% oxygen produced no improvement and a terminal cardiac arrest occurred at 05.45 hours.

Analysis of blood samples, the first of which was obtained 5 hours after ingestion of the solution, showed raised but nonlethal plasma and red cell hydrogen cyanide levels and a particularly high red cell gold concentration (Table 1). Plasma thiocyanate concentration was raised and continued to rise for a further 5 hours, whereas blood hydrogen cyanide levels declined after the dose of cobalt edetate.

Discussion

Ingestion of cyanide salts causes dizziness, drowsiness, nausea, vomiting, tachypnoea, tachycardia and hypotension. Following a lethal dose, coma, convulsions and death ensue within minutes. Cyanide acts by combining with the active site of the terminal respiratory enzyme, cytochrome a_3, thus inhibiting cellular aerobic respiration.[1] Anaerobic glycolysis therefore proceeds at an increased rate, whilst oxygen utilisation falls, producing severe lactic acidosis and a decreased a-$\bar{v}$ oxygen difference.

This patient developed some features of cyanide poisoning but these did not appear until about 5 hours after ingestion of the gold solution which contained 540 mg of cyanide (> 5 times the lethal dose) in the form of $Au(CN)_2^-$. Moreover, we would consider her blood hydrogen cyanide levels at this time to be sublethal since they compare with some high, but nonsymptomatic cyanide concentrations in patients infused with the hypotensive agent, sodium nitroprusside.[2,3] In addition, the patient's clinical condition deteriorated only after the injection of cobalt edetate which actually reduced her blood cyanide concentration. For these reasons we think it unlikely that HCN was the primary toxic agent.

The toxic effects of gold salts when chronically administered to arthritics are well known and manifest as dermatitis, renal damage and bone marrow depression.[4] However, acute gold cyanide toxicity has rarely been reported.[5] Experimental studies in rabbits showed that an intravenous dose of 15 mg/kg was lethal and 10 mg/kg caused dyspnoea, convulsions and paralysis with recovery after 10 minutes. Toxicity was also noted in patients treated with $KAu(CN)_2$ for cutaneous tuberculosis and syphilis.[6]

The ratio of red cell : plasma gold concentration in this patient is noteworthy. Studies of arthritics administration of nitrous oxide to pregnant patients does not cause fetal abnormalities, or lead to an increased incidence of abortion or of low infant birth weight.

The authors' series is small and they recognise that with it they would not have been able to detect abnormalities which occurred only rarely. Unfortunately, no other study has compared the outcome of pregnancy in patients who received nitrous oxide for operation with a population having similar procedures but anaesthetised with other agents. Two recent studies have examined the subject of operation during pregnancy. One is the case-control study by Duncan *et al.*[7] which surveyed the entire Manitoba population (approximately 1 million) between 1971 and 1978 using health insurance data. A series of 2565 women undergoing operation during pregnancy were matched to a similar number of nonoperated controls by maternal age and area of residence. The type of anaesthesia was categorised only as nil (18%), general (57%), spinal block (2%) or local (24%). Thus, one can only conjecture that nitrous oxide was administered to the majority of patients having general anaesthesia and that most of the major surgical procedures were performed using general anaesthesia. Duncan *et al.*[7] found that the incidences of congenital anomalies and of abortions were the same in the operated and nonoperated groups. When data for the different anaesthetics were compared with each other, they found a greater incidence of first and second trimester spontaneous abortions (most notably for gynaecological procedures) in those having general anaesthesia. A study by Brodsky *et al.*[8] compared questionnaire data from 287 pregnant dental personnel and wives of dentists who underwent operation with general anaesthesia with data from a nonoperated control group. No specific information was given regarding the anaesthetic agents that were employed or the operations that were performed. They found no association between operation during pregnancy and congenital anomalies in the offspring, but the incidence of fetal loss during pregnancy was greater in the operated group.

In summary, definitive clinical studies in this area have not yet been done. The study by Crawford and Lewis is too small to detect subtle effects and the other studies have not addressed the issue of the use of nitrous oxide for operation during pregnancy. Nevertheless, the information we have and the absence of case reports documenting adverse developmental effects lead to the conclusion that the incidence of congenital anomalies among the offspring of women who undergo anaesthesia and operation while pregnant is not increased. Thus, the biochemical data derived from human and animal studies, although valid, do not appear to be predictive and one can conclude that it is safe to administer nitrous oxide to pregnant women. (This should be qualified by saying, for single procedures lasting less than 6 hours.) Because the risk of congenital anomalies is not increased, there is no indication to pretreat pregnant women with folinic acid before administration of nitrous oxide. There are even fewer data from which to draw conclusions regarding the relationship of the administration of nitrous oxide to the incidence of first and second trimester spontaneous abortion. However, most studies suggest that the underlying disease process, (e.g., cervical incompetence, appendicitis) which lead to the operation is a far more significant risk factor than the choice of anaesthetic agent. Thus, the chance of inducing spontaneous abortion should not deter the anaesthetist from administering nitrous oxide to pregnant patients. Until data are presented to disprove these views, the continued use of nitrous oxide during pregnancy is rational.

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R.I. MAZZE

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undergoing chrysotherapy[4,7] have revealed higher ratios in smokers (0.35) than in nonsmokers (0.028) and the implication that inspired HCN in tobacco smoke facilitates the entry of gold into the red cells has been confirmed by *in vitro* studies. These suggest that $Au(CN)_2^-$ rapidly penetrates the red cells and cyanide acts as a 'shuttle' for the gold.[8] The ratio of red cell: plasma gold in this patient (16.7) was thus very much higher than that seen in arthritic smokers receiving gold treatment and suggests enhanced cellular uptake of gold because it was ingested as the cyanide. At the cellular level, (Au[1]) is known to penetrate the lysosomal, mitochondrial and nuclear membranes and to show affinity for cysteine residues in protein.[9,10] It thus inhibits a number of enzymes including, most significantly, the enzyme rhodanese[11] which converts HCN to the virtually non-toxic SCN. Rhodanese (thiosulphate: cyanide sulphurtransferase EC 2.8.1.1), a mitochondrial enzyme, utilises sulphane sulphur, e.g. thiosulphate, as a substrate for cyanide detoxication.[12] This mechanism is adequate for dealing with 'normal' cyanide exposure, for example in smokers in whom plasma thiocyanate levels are consequently raised (plasma thiocyanate mean, (SD) 141 (43) compared with nonsmokers, 42 (22) μmol/litre),[13] but is limited by the supply of thiosulphate in acute cyanide poisoning.[14]

Our patient, who was a nonsmoker, showed a raised plasma thiocyanate level of 91 μmol/litre 5 hours after taking the gold cyanide solution. Thus, considering both the quantity of cyanide ingested and the blood cyanide level before cobalt edetate was given, the rise in thiocyanate was slower than might be expected. Following treatment with cobalt edetate and the consequent reduction in blood cyanide levels, the rate of increase in plasma thiocyanate was naturally reduced. Assuming a body weight of 60 kg, a rise in plasma thiocyanate from an assumed, nonsmoker level of 42 up to 91 μmol/litre and a thiocyanate space of 210 ml/kg, it can be calculated that detoxication of only about 3.5% of the cyanide in the ingested solution occurred over the course of the first 5 hours. This was probably due to inhibition of rhodanese by the gold.

In the absence of cyanide, cobalt edetate is known to produce anaphylactic reactions, oedema, atrial fibrillation, hypocalcaemia and hypomagnesaemia.[15-20] However, the clinical course was not that of a lethal anaphylactic reaction: the patient did not display gen
oedema, bronchospasm or immediate
tension, nor did the CoEDTA cause
calcaemia. We feel, therefore, that cobalt
is unlikely to have contributed to her d
view of the high red cell gold levels and
inhibition of rhodanese (presumably pa
by inhibition of other intracellular enzy
believe that gold was the principal leth
and that its action was enhanced by
cyanide.

This case also raises certain issues ab
treatment of cyanide poisoning. It is
imperative to implement treatment imme
when patients are known to have i
cyanide. A heparinised blood sample sh
obtained for blood gas analysis and
assay, and antidotes, together with
oxygen[21] and general supportive m
quickly given. Indeed, supportive meas
themselves have proved effective, even
large amounts of cyanide have been ingest

In massive cyanide poisoning, as in in
accidents, CoEDTA is the best antidot
it has a rapid action and, althoug
alone, combines with HCN to form a
nontoxic complex.[15] However, if a patien
conscious some hours after assumed exp
cyanide, cobalt edetate is not the treat
choice.

In the clinical situation, where patien
have survived for some time before ar
hospital, or where there is some question a
toxic agent or the amount ingested, thiosu
the nontoxic and physiological subst
rhodanese, is the preferred antidote.
especially indicated when cyanide toxicit
to sodium nitroprusside overdose[24,25] a
be given in large and repeated doses.

The nitrites, despite their vasodilati
therefore hypotensive action, may be a
adjunct to thiosulphate in acute cyanide
ing (although not in patients infused with
nitroprusside). Their mode of action is to
haemoglobin to methaemoglobin, the fer
(Fe^{3+}) of which combines with cyanide,
reversing the inhibition of cytochro
Sodium nitrite (3%) is injected in 10 ml d
convert around 25% of haemoglobin to
moglobin, and is much more effective tha
nitrite. However, the decreased oxygen
to the tissues presents a further hazar
ticularly to children.[26] It is doubtful

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Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; 1: 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 12 December 1986 for April 1987; 13 March 1987 for June 1987 and 12 June 1987 for September 1987.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

nitrites were indicated in this case because of hypotension.

In summary, cyanide ingestion is usually lethal if not treated rapidly. In retrospect it would seem that gold toxicity played the major part in the death of our patient and dimercaprol might have prevented this.[27] In addition, thiosulphate administration, besides aiding cyanide detoxification, would have had the added virtue of assisting the reversal of gold-induced enzyme inhibition as it does in platinum toxicity.[28]

Acknowledgments

Plasma and whole blood gold concentrations were determined by atomic absorption spectrometry by Dr B. Widdop and colleagues at the Poisons Unit, New Cross Hospital, London. We thank Dr M. Farthing and Dr C.J. Hinds for permission to report on a patient under their care.

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Nitrous oxide in early human pregnancy

J. S. CRAWFORD AND M. LEWIS

Summary

An analysis of the outcome of 375 cases (383 fetuses) of cervical cerclage and 58 other operations (59 fetuses) conducted under general anaesthesia, which included the administration of nitrous oxide, failed to reveal a single instance of which nitrous oxide could have been clearly indicted as a cause of fetal abnormality The incidence of inevitable abortion and of low birth weight babies in the series of cervical cerclage conducted under general anaesthesia was identical to that in a series conducted under regional analgesia (115 fetuses). This represents the first of a two-part test of the proposition that nitrous oxide should not be administered to women in the first or second trimester. Our interim conclusion is that the proposition is unacceptable.

Key words

Anaesthetics, gases; nitrous oxide.
Pregnancy; abortion, teratogenicity.

It has recently been suggested that because of the known effect of nitrous oxide on DNA synthesis, the gas should not be used during the first two trimesters of pregnancy.[1] This is based on the observation that when rats are exposed to nitrous oxide for prolonged periods, and when humans are exposed to the drug for either prolonged periods or intermittently during the course of several days or weeks, among other responses inactivation of methionine synthetase occurs although, apparently, to a lesser extent in humans than in rats. This results in an interference with folate metabolism and thus an impairment of DNA synthesis. Recovery of the capacity, by rats, to synthesise DNA following depletion of methionine synthetase is measured in days. It has been suggested that folinic acid, given prophylactically, may avert the dangers which have been attributed to nitrous oxide.[1]

Because of the important implications regarding the use of nitrous oxide in the first two trimesters of pregnancy, it is important to study the validity of this contention in the clinical situation. There are two ways in which this may be achieved: a series of women known to have received nitrous oxide early in pregnancy can be identified and the outcome of each pregnancy defined appropriate to the hypothesis; a series of progeny with congenital malformations can be identified and evidence sought to discover how many of the mothers concerned had received nitrous oxide early in the relevant pregnancy.

Here we present the results of our application of the former approach. Currently, we are

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CASE REPORT

Bronchospasm following the use of vecuronium

A. C. O'CALLAGHAN, G. SCADDING AND J. WATKINS

Summary

A case history is presented which records bronchospasm due to vecuronium. Immunological investigations, including basophil degranulation tests, indicated that the bronchospasm was not caused by direct histamine release and was not IgE mediated. It was of interest that intradermal testing gave a positive wheal response against neuromuscular agents other than those involved in the anaesthetic procedure under investigation. A positive reaction to vecuronium was only obtained when given in a high concentration and accords with the general belief that vecuronium has extremely low potential for histamine release.

Key words

Complications; bronchospasm.
Neuromuscular relaxants; vecuronium.

Vecuronium has been promoted as an agent that does not cause histamine release in clinical doses.[1] Since its introduction there has been one case report of anaphylactic shock including bronchospasm[2] and two communications[3,4] of possible histaminoid reactions, both manifested by skin rashes and in one case accompanied by severe hypotension. This case history reports an allergic reaction to vecuronium manifested by bronchospasm and details the results of immunological investigations on blood samples taken during and after the reaction and the results of intradermal testing.

Case history

A 66-year-old man was scheduled for cystoscopy and dormia basket extraction of a stone low in the right ureter. Significant past medical history included two ureterolithotomies with no anaesthetic problems. The patient had no history of cardiac disease, asthma or obstructive airways disease. He was receiving no medication. There was a history of a penicillin allergic reaction which he described as a rash. He was a nonsmoker. On examination, he was obese (92.5 kg and height 1.75 m), but had no other abnormal physical signs. Pre-operative chest X ray and electrocardiogram were normal. Blood haematology analysis and blood chemistry were also normal.

The patient was premedicated with papaveretum 15 mg, hyoscine 0.3 mg and perphenazine 2.5 mg intramuscularly. He was found to be sedated on arrival in the anaesthetic room. Anaesthesia was induced with thiopentone 450

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engaged in initiating the second approach and the results of that study will be submitted later.

Methods

The case record of every woman who received general anaesthesia (which invariably included the provision of nitrous oxide in an inspired concentration of at least 33%) in the Birmingham Maternity Hospital (from its opening in 1968) during the first two trimesters of pregnancy was scrutinised. The records of every woman who received a general anaesthetic (which included nitrous oxide in a higher inspired concentration) during early pregnancy in the Birmingham and Midland Hospital for Women during a similar period, and was delivered (or aborted) in the Maternity Hospital, were similarly scrutinised. During this period 12 women operated on in early pregnancy in the Women's Hospital were not delivered in the Maternity Hospital, and they have been omitted from further consideration.

Note was made of: the category of operation; the gestational age at the time of anaesthesia; the duration of administration of anaesthesia; any other volatile anaesthetic agent concurrently administered; the gestational age at the time of delivery (or of abortion); the birth weight and sex of the infant(s); evidence at the time of delivery, or subsequently, of malformation.

A large percentage of the operations were cervical cerclage (either Shirodkhar or Macdonald suture). As many of these procedures are conducted under regional analgesia (either spinal or lumbar epidural), it was considered potentially interesting to collect from this series data comparable to those outlined above.

Results

The pertinent data are summarised in Table 1. General anaesthesia (mean duration 37.6 minutes; range 15–80 minutes) was given to 58 patients (including one with a twin pregnancy) for operation other than cervical cerclage (Table 2). Thirty-four of these (involving 35 offspring) were conducted before the completion of organogenesis (16 weeks gestation), and in this group there was one case of congenital defect: a child with mitral stenosis who died at 6 weeks of age. This lesion originated in maldevelopment initiated at 4–6 weeks gestation, that is, before the mother was exposed to nitrous oxide.

There were three children with defects from the mothers exposed to nitrous oxide subsequent to 16 weeks gestation: rhino-orodigital syndrome (an autosomal dominant mutation); trisomy 18. These were manifestly unrelated to nitrous oxide. Thirdly, there was a child with an undescended testis, a condition which is considered to reflect abnormal hormonal influence. None of the patients in this series aborted.

A cervical cerclage was inserted under general anaesthesia in 375 cases (Table 3), including eight women with a twin pregnancy. The mean duration of anaesthesia was 22.3 minutes, range 10–65 minutes. Anaesthesia was provided for 294 mothers (four with a twin pregnancy) before completion of the 16th week of pregnancy, and among these the following anomalies subsequently became apparent: three cases of neural tube defect (the neural tube is normally closed by the end of the 5th week of pregnancy; these three women received general anaesthesia during the 12th, 13th and 14th week respectively); an Ellis van Crefeld syndrome (a recessive inherited disease); hypothyroidism in one twin (the possibility that nitrous oxide could have been instrumental in causing this appears to be extremely remote); two cases of inguinal hernia, one infant with a retractable testis, one with chordee penis and one with pyloric stenosis

Table 1. Summary of the information detailed in the subsequent tables

	Number of fetuses		Abortions	Low birth weight infants	Congenital anomalies
General anaesthesia for other than cervical cerclage	At ≤ 16/52	35	Nil	Nil	1
	At > 16/52	24	Nil	1	3
General anaesthesia for cervical cerclage	At ≤ 16/52	298	28	6	10
	At > 16/52	85	9	5	4
Regional analgesia for cervical cerclage	At < 16/52	96	9	3	7
	At > 16/52	19	2	1	Nil

mg and muscle relaxation provided with suxamethonium 100 mg. Following laryngoscopy and topical spray with 200 mg lignocaine, the trachea was intubated with a size 9.0 Magill cuffed oral tracheal tube. The position of the tracheal tube was checked and ventilation found to be equal on both sides. Anaesthesia was maintained with 70% nitrous oxide in oxygen with inspired halothane 1–2%. Following institution of an intravenous infusion of Hartmann's solution, vecuronium 8 mg and fentanyl 0.1 mg were injected into the intravenous tubing using two separate syringes with two separate needles. The patient's lungs were ventilated by a Manley ventilator, provided with a fresh gas flow of 10 litres/minute. The inspiratory bellows pressure was set at 2.5 kPa and the inspiratory tidal volume was adjusted to 800 ml. On listening again to the patient's chest after injection of vecuronium and fentanyl, expiratory wheezing was noted which lasted for a few minutes and resolved spontaneously. During this period ventilation was not impaired by the bronchospasm. The surgeons were unable to extract the stone by dormia basket and decided to proceed to right ureterolithotomy and retropubic prostatectomy.

Approximately 45 minutes after the first dose of vecuronium, neuromuscular monitoring using a train-of-four stimulus indicated that the patient required a further dose of muscle relaxant; vecuronium 8 mg was therefore given. Two minutes later the patient developed marked inspiratory and expiratory wheezing, first noted by the ventilator failing to deliver the set tidal volume despite an increased inflation pressure of 3.5 kPa applied to the bellows of the Manley ventilator. Intravenous aminophylline 150 mg was given slowly but the patient showed no improvement. A problem with the tracheal tube was suspected so it was changed to a size 9.0 cuffed tracheal tube (Portex). On inspection of the tracheal tube after its removal there was no obstruction of the lumen or overinflation of the cuff. The patient's bronchospasm did not resolve after changing the tracheal tube. The tube position was rechecked; both lungs were ventilated equally with no clinical signs of a pneumothorax. On gentle suction of the tracheal tube there was no evidence of aspiration of stomach contents. Hydrocortisone 200 mg was given and a further 50 mg of aminophylline. Thirty-five minutes after the second injection of vecuronium the bronchospasm had decreased to expiratory wheezing only. The patient's cardiovascular state had been stable during this period.

One hundred and five minutes after the second injection of vecuronium the results of train-of-four nerve stimulation indicated that a further dose of muscle relaxant was required and vecuronium 4 mg was given. Within 3 minutes the bronchospasm had increased again but responded to 50 mg aminophylline given slowly. Blood samples were taken into EDTA (ethylene diamine tetracetic acid) bottles for complement, immunoglobulin assay, haematocrit, differential white blood cell count and a clotting screen.

The neuromuscular block was reversed 32 minutes after the third injection of vecuronium with neostigmine 2.5 mg and atropine 1.2 mg and the patient had no further problems. A total of 1300 ml of Hartmann's solution was infused peroperatively over a period of 2 hours and 40 minutes. Chest X ray in the recovery room showed clear lung fields with no evidence of a pneumothorax or pulmonary oedema.

Further blood samples were taken at 3, 6 and 24 hours. The blood for complement and immunoglobulin assay was centrifuged, the plasma separated and stored at minus 20°C until it was despatched to the Protein Reference Laboratory at Sheffield. Skin tests were performed 6 weeks later according to the protocol of Fisher[5] and 50 ml of blood taken for a basophil degranulation test.[6]

Results

Total leucocyte count had increased from 5.2×10^9/litre to 22.5×10^9/litre, but there was no change in the polymorph/leucocyte ratio. Haematocrit was unchanged at 45% and at 24 hours it was 42.2%. Clotting studies were normal.

Immunoglobulins IgG, IgA, IgM and IgE levels did not change in the samples taken at the time of the reaction or at 3, 6 and 24 hours later. The results were in the normal range except for the plasma IgE level at 15 IU/ml, which is well below the median population value of 60 IU/ml. The complement factors C_3, C_4 C_3PA and C_1 inhibition factor remained stable in the four blood samples taken over the 24 hours following the suspected allergic reaction.

Intradermal testing of the anaesthetic agents used and the common neuromuscular blocking agents with saline and histamine controls revealed positive allergic responses to each of

Table 2. Pertinent data from 58 operations other than cervical cerclage conducted under general anaesthesia

Gestational age at operation (weeks)	*N*	Operation (duration of anaesthesia in minutes) (abnormalities)
8	1	ov. cyst (30)
9	2	ov. cyst (35); laparoscopy (25)
10	2	ov. cyst (35); ov. cyst (35)
11	2	ov. cyst (25); removal of fibroid (34)
12	2	ov. cyst (30); appendicectomy (60)
13	4	ov. cyst (40); ov. cyst (55); laparotomy (25); ov. cyst (55)
14	5	ov. cyst (30); ov. cyst (30); salpingo-oophorectomy (40); laparotomy (20); laparotomy (20)
15	9	ov. cyst (47); ov. cyst (80); ov. cyst (40); ov. cyst (30); ov. cyst (45); ov. cyst (30); ov. cyst (45); salpingo-oophorectomy (30); appendicectomy (30) (CHD/NND)
16	7	ov. cyst (25); ov. cyst (35); ov. cyst (30); ov. cyst (35); ov. cyst (15); ov. cyst (15); appendicectomy (25)
17	3	ov. cyst (43); ov. cyst (30); antero-version (20)
18	2	appendicectomy (45); appendicectomy (45)
19	Nil	
20	5	ov. cyst (40); (rhino-oro-digital syndrome); appendicectomy (25); appendicectomy (45); appendicectomy (30); appendicectomy (65) (one undescended testis); appendicectomy (30)
21	Nil	
22	3	ov. cyst (35); fimbrial cyst (35); appendicectomy (30)
23	Nil	
24	4	ov. cyst (40); appendicectomy (40); appendicectomy (35) (LBW); release of trapped nerve of thigh (45) (trisomy 18)
25	5	ov. cyst (45); ov. cyst (35); appendicectomy (40); appendicectomy (35); appendicectomy (55)
26	2	appendicectomy (50); appendicectomy (50)

Ov. cyst: ovarian cystectomy; LBW: low birth weight infant; CHD/NND: congenital heart disease, died aged 6 weeks.

(informed opinion obtained in personal communication from perinatal pathologists is that the possible relationship between maternal exposure to nitrous oxide and any of these conditions is so remote as to be virtually nonexistent).

Among the infants whose mothers had undergone cervical cerclage under general anaesthesia subsequent to 16 weeks gestation were four with congenital anomalies: Potter's syndrome in one of twins (the progress of this defect is initiated early in the first trimester); exomphalos (extension of the coelom into the umbilical cord is normally obliterated by the end of the 12th week of gestation); micrognathia (the mother had had four previous inevitable abortions, and this case almost certainly reflected a continuum of reproductive defection); congenital laryngeal stridor (development, as distinct from maturation, of the larynx is completed during the first trimester).

The incidence of inevitable abortion subsequent to cervical cerclage was understandably high, in view of the obstetric pathology. Eleven women aborted within 2 weeks after the operation and 25 (including one with twins) after a longer interval. One pregnancy ended with a stillbirth at 31 weeks (permission for autopsy refused) and there were 11 low birth weight infants. Three infants delivered very prematurely died in the neonatal period, and another was a cot death. The total incidence of abortion relating to this series of 383 fetuses was 9.7% and among the remaining 346 infants 11 (3.2%) were low birth weight.

Cervical cerclage was inserted under regional analgesia in 114 cases (including one twin pregnancy) (Table 4). Among the 95 cases operated on prior to the completion of 16 weeks pregnancy, the following anomalies subsequently became apparent; a child with disproportionately short limbs; ventriculoseptal defect; partial syndactyly; umbilical hernia; pyloric stenosis; a child with an accessory auricle and another with an accessory nipple.

Three women aborted within 2 weeks of the operation. The total incidence of abortion tubocurarine, atracurium and pancuronium at a 1:1000 dilution and to vecuronium only at a 1:10 dilution. The basophil degranulation test showed no release of histamine with dilutions of vecuronium ranging from 1/100000 to 1/10.

Discussion

This paper reports bronchospasm which developed after the use of vecuronium. In each episode the signs occurred within a few minutes of intravenous administration of the drug and increased on subsequent exposures. The results of the investigations contrast with the previous communications of Clayton[3] and Lavery *et al.*[4] in which either immunoglobulin analysis or intradermal testing were performed but not both together.

In our patient the haematology data show an increase in the total leucocyte level which is common to the stress response to any surgical and anaesthetic trauma. Marked changes in polymorph/leucocyte ratio (neutrophilia) occur only if complement is activated. The lack of complement involvement and stability of immunoglobulins and haematocrit over the 24-hour period demonstrate minimal plasma protein disturbance and fluid shift.

The positive skin reactions obtained with 1/1000 dilutions of tubocurarine, atracurium and pancuronium and a 1/10 dilution of vecuronium indicate that these non-depolarising neuromuscular blocking agents all provoke histamine release in this patient. It is noteworthy that vecuronium had a higher threshold for triggering a positive reaction compared to the other relaxants tested. Moneret-Vautrin *et al.*[7] have shown by skin testing that crossed reactions to vecuronium can occur and suggest that it may be possible to induce anaphylactic shock at the time of first exposure to vecuronium in patients who have been sensitised to other muscle relaxants. However, the basophil degranulation test did not indicate antibody involvement in this case.

The low plasma IgE level of 15 IU/ml does not indicate a tendency to immunological sensitivity. It might indicate a non-immune tendency to react to rapid bolus injection of intravenous drugs, particularly the neuromuscular blocking compounds.[8] The mechanism of production of bronchospasm in this patient is not known, but the lack of histamine release on *in vitro* testing and the high threshold for intradermal reactivity are not suggestive of histamine release. It is possible that a metabolite of vecuronium was responsible and that *in vivo* metabolism is required before histamine is released. Direct activation of the alternative pathway of complement is an unlikely mechanism since C_3 values remained stable. Possibly, direct activation of plasma kinins was responsible.

Despite vecuronium not being completely free from histaminoid response, the intradermal reactions were less severe than with the other non-depolarising neuromuscular blocking agents tested. Premedication with H_1 and H_2 antagonists is recommended if the use of a muscle relaxant is indicated in a patient known to be sensitive to neuromuscular blocking drugs.[8] It is important to note that adverse reactions can still occur with this new muscle relaxant which has a low potential for histamine release.

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Table 3. Pertinent data from 375 cases of cervical cerclage conducted under general anaesthesia.

Gestational age at operation (weeks)	*N*	Abnormalities
7	3	Nil
8	9	ab (10,12,13, 16/52); retractable testis
9	13	ab 13/52
10	22	ab (10,15,17,23,24/52); Ellis van Crefeld syndrome; cot death at 6/52; LBW
11	16	ab (16,16,17/52), premature labour 25/52, with NND
12	47	ab (13,16,16/52), meningo-myelocoele; pyloric stenosis; LBW
13	39	ab (19, 20/52); stillbirth 31/52; LBW; meningo-myelocoele
14	65	ab (16,20,22,22,26,27/52); spina bifida; chordiae penis; inguinal hernia, LBW
15	41	ab (19,23,24/52); LBW; LBW; inguinal hernia; spontaneous labour 26/52 (NND)
16	39	ab 24/52; hypothyroid in one twin; stillbirth (prolapsed cord)
17	7	LBW
18	17	ab (24,25/52); neonatal death 26/52; micrognathia; exomphalos
19	10	ab (19,22/52); LBW
20	19	ab (21,22/52); LBW, LBW
21	2	ab 22/52
22	6	congenital laryngeal stridor; spontaneous labour 28/52 (NND)
23	1	Nil
24	8	ab 24/52; LBW
25	4	ab (25, 25/52)
26	3	Potter's syndrome in one twin
27	2	Nil
28	1	Nil

LBW: low birth weight infant; NND: neonatal death; ab: inevitable abortion at indicated week of gestation.

Table 4. Pertinent data from 114 cases of cervical cerclage conducted under regional analgesia

Gestational age at operation (weeks)	*N*	Abnormalities
9	3	Nil
10	3	ab (21/52)
11	0	
12	16	ab (15/52); LBW 29/52; disproportionately short limbs; accessory auricle
13	25	ab (18,21/52); pyloric stenosis
14	23	ab (18,21,23/52); spontaneous labour 25/52; accessory nipple; LBW
15	13	ab (15,16/52); LBW; V.S.D.
16	12	spontaneous labour 25/52; partial syndactyly; umbilical hernia
17	6	ab (21/52)
18	3	LBW
19	2	Nil
20	1	Nil
21	0	—
22	4	Nil
23	0	—
24	1	ab (24/52)
25	1	Nil
26	0	—
27	0	—
28	1	Nil

LBW: low birth weight infants; VSD: ventriculoseptal defect; ab: inevitable abortion at indicated week of gestation.

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APPARATUS

The current status of pulse oximetry

Clinical value of continuous noninvasive oxygen saturation monitoring

M. B. TAYLOR AND J. G. WHITWAM

Summary

The history of the development of pulse oximetry is outlined and the principle of how the apparatus works is described. The instrument detects hypoxic hypoxia and the shape of the oxygen dissociation curve means that the minimum saturation alarm should be set at 94% in anaesthetic usage. It is accurate to within 2% and is usually unaffected by racial pigmentation, but accuracy can be affected in low perfusion states, hypothermia and in the presence of abnormal forms of haemoglobin and pigments in the blood. Its clinical evaluation in the operating theatre and intensive care unit is reported. It was found to be useful and reliable and would appear to have logistical and other advantages over current methods of detecting hypoxia. Pulse oximetry may make a significant contribution to the safety of anaesthetic practice.

Key words

Measurement techniques; pulse oximetry.

Tissue hypoxia is a major cause of morbidity and is ultimately the cause of death in most humans. One cause of tissue hypoxia is a failure of oxygen delivery which depends on the oxygen supply, lung function, cardiac output and the oxygen capacity and affinity of the blood which, in turn, depends on the concentration of functioning haemoglobin and its P_{50}. Until recent years the assessment of oxygenation of blood has depended on invasive intermittent blood gas analysis or indwelling polarographic electrodes.

The first noninvasive measurements of the percentage of oxyhaemoglobin (i.e. oximetry) in man, were in the ear and hand,[1] although oximetry had previously been used on exposed blood vessels in 1934.[2] During the next two decades noninvasive oximetry was developed for many purposes, including cardiac output measurements.[3] However, these systems were technically difficult to use, they measured the total tissue absorption of an incident electromagnetic spectrum and were difficult to calibrate without invasive blood sampling.[4,5]

The development of rapid, reliable methods of measuring the oxygen tension of blood by the adaptation of the Clark polarographic electrode[6] in the 1950s led to a decline of interest in oximetry. In recent years the polarographic electrode has been adapted for noninvasive, continuous measurement of transcutaneous oxygen tension which is arterialised by the use of heat. However, this noninvasive system is not entirely satisfactory and it has recently been suggested that the physiological response time is too slow to

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relating to the series of 115 fetuses was 9.6% and among the remaining 104 infants, 4 (3.8%) were categorised as low birth weight.

Discussion

There are several studies relating to the possibility that surgery conducted under general anaesthesia during pregnancy has a detrimental effect upon the conceptus (embryo or fetus). There is some evidence that such procedures, when undertaken during early pregnancy, might be associated with an increased likelihood of abortion.[2] However, it is likely that the site of the surgical procedure is the major determinant in this regard. Also, it is notoriously difficult to gather accurate information regarding the incidence of abortion within a community, and such difficulty is greatly compounded when reliance is placed upon a postal survey[2] or nationally accumulated statistics.[3,4] Indeed, the figures quoted in any of the cited reports must be regarded in the light of current understanding that approximately 40% of pregnancies end in spontaneous abortion and that it is likely that, in the absence of specific investigations, in half of such cases the mother will not have realised that she had conceived.[5] These facts appear not to have attracted the attention of many of the anaesthetists who express concern about the dangers associated with atmospheric pollution.

The situation is less uncertain in regard to the possibility that such a procedure, conducted in the first (or second) trimester, entails the risk of causing fetal abnormality. In none of the studies cited was an associated increase in the incidence of fetal abnormalities found. Specifically, Duncan and colleagues,[4] whose data derived from a survey of the entire population of Manitoba, found that the incidence of anomalies among 2565 pregnancies in which a surgical procedure had been performed in the first or second trimester was 1.68%, and that among a similarly sized group of controls was 1.52%. Shnider and Webster, reporting on personally collected data (the series thus being necessarily smaller), found a 3.44% incidence of birth defects among 105 pregnancies.[3] In 47 of these, a surgical procedure had been performed in the first trimester, in the remainder during the second, compared with 6.03% among a hospital-based series of 8926 controls.

In the present series, the incidence of abnormalities among pregnancies in which general anaesthesia had been administered during the first 16 weeks (excluding cases of abortion) was 3.6%, whereas it was 8.0% among cases which had been conducted under epidural analgesia during the same gestational period.

However, the percentages referred to must be viewed with considerable reserve, as each represents an accumulation derived from quite disparate sources. They contain no reference to the specific abnormalities within the review series, to familial defects within the community studied (including the closeness of consanguinity of the parents), or to the ethnic origin of the parents. Furthermore, minor defects (such as webbed digits or a slight degree of hypospadias) could well not have been drawn to the attention of those who have conducted a large survey. Similarly, there might have been a local epidemic (for example, rubella or influenza) during the pertinent period of the survey. In addition, some abnormalities will subsequently be revealed only by chance (for example, an abnormally low level of cholinesterase activity, or susceptibility to malignant hyperpyrexia).

There is a considerable volume of published literature detailing evidence that exposure to nitrous oxide can inactivate methionine synthetase. Most reports, for understandable reasons, refer to experiments conducted upon animals and on tissue extracts. One of the most recent of such reports details the depression of methionine synthase activity in fetal and maternal liver when pregnant rats were exposed to relatively low concentrations of nitrous oxide for periods which varied from 30–240 minutes.[6] The extent of depression from the normal level of activity varied directly with the duration of exposure. The authors did not investigate the time required for full recovery after exposure, but did record that recovery was only partial 72 hours after nitrous oxide administration had been discontinued.

Koblin *et al.* reported one of the few studies of this phenomenon in human subjects.[7] They obtained liver biopsies from patients undergoing an abdominal operation, and assayed the methionine synthetase activity in the treated specimens. They found that, when compared with specimens obtained from patients who had not been exposed to nitrous oxide, there was a significant depression of activity in the material obtained from patients who had been exposed to accurately monitor rapid changes in arterial oxygenation during anaesthesia.[8,9] Technical developments in light sources and electronics have lead to a resurgence of interest in oximetry. It is now possible to differentiate the absorption of incident light by the pulsatile arterial component from the static component of tissue, hence the term pulse oximetry. Several instruments are now available for this purpose.

Principles and development of pulse oximetry

Principles

Cutaneous oximetry depends on absorption spectroscopy and all types of cutaneous oximeters depend on three physical principles for their operation and calculation of the arterial oxygen saturation of haemoglobin (Sao_2).

The differences in absorption spectra of reduced and oxygenated haemoglobin. These differences, which have been extensively investigated following the work of Vierordt,[10] are maximal in the red region at 640 nm wavelength. To calculate Sao_2, a second wavelength is required where absorption is different from the red region, e.g. in the infrared. The infrared is also used because, as in the red region, the absorption by haemoglobin is large in comparison to body tissue. An isobestic point, where oxygenation and reduced haemoglobin transmit light to the same degree occurs in the infrared region at 805 nm and this has commonly been used in oximeters as it makes the calculation of Sao_2 simple. However, this is not necessary if absorption coefficients are known and is not used in most pulse oximeters.

The Beer Lambert law is valid. This law states that at a constant light intensity and haemoglobin concentration the oxygen saturation of haemoglobin is a logarithmic function of the intensity of transmitted light through the haemoglobin sample. The use of a second wavelength enables calculation of saturation irrespective of the haemoglobin concentration, although this is only strictly true for haemolysed blood as absorption coefficients vary with the haemoglobin concentration of whole blood.

Reduced and oxygenated haemoglobin are the only forms present in blood. As other species of haemoglobin may be present in blood, e.g. carboxyhaemoglobin and methaemoglobin, this assumption could lead to errors in the calculated Sao_2.

Equipment

Pulse oximeters, which were first develop
Japan,[11] consist of a probe, a microprocess
display components.

Probe. The probes, which may be design
fingertip or earlobe application, are either
optic[12] transmitting filtered light from and
body of the instrument or, as found in
commercially available models, consist of a
two light emitting diodes and a photodetect
the Biox III (Ohmeda) the diodes produce
lengths of 660 and 940 nm and alternate o
off with each other at a frequency of 720 H
on, red off, infrared on, infrared off, etc)
photodetector is a nonspecific light detecto
produces outputs for the transmitted light
each of the diodes and also for any ambien
detected during the off periods in the 7
cycle. The Biox III probes have therm
controlled heating elements to stabilis
diodes and increase tissue perfusion, bu
probes on the newer Biox 3700 and on
makes of pulse oximeters are not heated
Biox 3700 has a small flexible probe wh
taped in position and this makes oximetry
sible on small children and neonates. We
found the standard ear and finger probe
suitable for children who weigh less than

Microprocessor. The principal proble
cutaneous oximetry is differentiating betwe
absorption of light due to arterial blood an
from all other tissue and blood in the light
Before pulse oximetry, solutions have u
involved taking initial standard light abso
readings from the tissue, made bloodless
pressure capsule, together with arterialisi
circulation during actual measurements wit
or histamine, to reduce errors from the pr
of venous and capillary blood. In ideal ci
stances accuracy was high, but the procedu
complex and calibration against arterial
saturation was needed for reliable absolute
ings of Sao_2.[4,5]

Pulse oximetry solves this problem by
tronically resolving the output from each
diodes, detected by the photodetector, into
alternating current (which detects absorpti
to the pulsating component in the tissu
arterial blood vessels) and direct c
(which detects absorption due to nona
blood and tissue, Figs 1 and 2). The DC p
the signal is electronically discarded and th

nitrous oxide (50–70%) for 1.25–2.75 hours. The nature of the study precluded attempts to assess the duration of depression of activity.

The results of these studies and others provide acceptably firm evidence that nitrous oxide, administered in an 'anaesthetically appropriate concentration', can depress enzyme activity. As far as we are aware, no evidence has yet been presented to suggest that such exposure, for a period approximate to that required for a surgical procedure, has proved deleterious to a human (or, indeed, an animal) subject. Still less has there been evidence of such a relationship with fetal development.

Although, for the sake of completeness, in this review of our experience we attended to the prevalence of low birth weight infants, we are well aware of the irrationality of the proposition that low birth weight could be related to the brief exposure of the fetus to nitrous oxide. We were induced to include such a survey by the use, in the statement by Nunn and Chanarin, of the phrase 'the first two trimesters'.[1] We believe that it would be advantageous if, in future debate, attention were concentrated upon the first 16 weeks of gestation.

Applying that limitation, our survey showed that of the 305 (live born and still born) infants delivered of mothers who had received nitrous oxide within the first 16 weeks of pregnancy, none had a defect which could be related to the drug. No case of abortion followed general anaesthesia given for any procedure other than cervical cerclage. The related incidence of subsequent abortion after cervical cerclage was almost precisely the same among women who had been given general anaesthesia as among those whose cerclage was conducted under epidural analgesia (we are unaware of any suggestion that brief exposure to bupivacaine might be detrimental to fetal development). It is possibly of interest to record that 364 of the women who comprised the total series received a volatile anaesthetic agent in addition to nitrous oxide; either halothane (187), trichloroethylene (132), methoxyflurane (43) or enflurane (2).

The series reported here is admittedly small. The results, however, give no support to the postulate quoted at the beginning of this communication. Additionally, it is never possible to prove a negative and we appreciate that investigation, similar to this, of a very large number of appropriately defined cases will be required to provide an acceptable verdict regarding the validity of the contention under review. We urge others with access to the relevant information to contribute to the accumulation of such data. The second part of our own survey, currently being undertaken, should also be of help.

In the meantime, we are of the opinion that the stricture that women in the first or second trimester should not be exposed to nitrous oxide, unless they have received prior medication with folinic acid, represents an unwarrantable cause of stress and anxiety among women of childbearing age and their medical attendants.

Acknowledgments

We are grateful to the staff of our Medical Records Department for the prompt retrieval of the several hundreds of case notes relating to pregnancies and operations during the period 1968–85.

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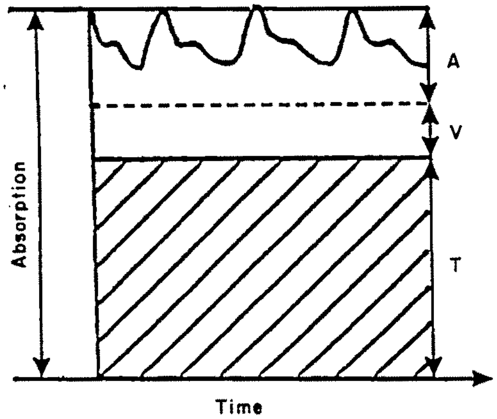

Fig. 1. Diagram of absorbance and modulation of incident light through body tissue, as detected by oximeter photodetector. A, arterial plethysmographic modulation; V, absorption due to venous and capillary blood; T, absorption from other tissue.

plethysmographic, part is digitised and further processed by means of derivatives of the equations derived by Wood *et al.*[13] The absorption coefficients used as constants in these equations are a potential source of error. The instantaneous saturation is averaged over a short time interval, e.g. 3–6 seconds, which produces a rapid response time together with a stable reading and reduction in probe movement artefact. Ambient light is compensated for, except when infrared heating lamps are in use.[14] No user calibration is required, warm up time is short and skin preparation straightforward.

Display. The display includes $S\mathrm{ao}_2$ pulse rate, alarms and usually some indication of the detected plethysomographic pulse signal, a subject which has recently been reviewed.[15]

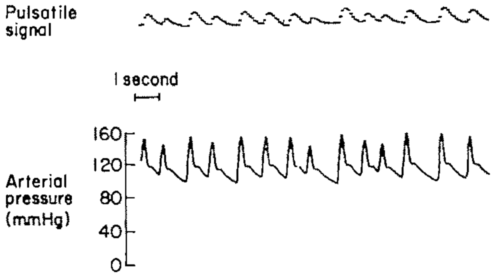

Fig. 2. Simultaneous recordings of pulsatile (plethysmographic) output signal from Biox III oximeter using ear probe, and left radial arterial pressure. The patient is in atrial fibrillation and $S\mathrm{ao}_2$ was reading 98%. No calibration of pulsatile output is possible.

Accuracy of pulse oximetry

The accuracy of pulse oximeters has been evaluated in normal adults breathing varying inspired concentrations of oxygen down to an $F\mathrm{IO}_2$ of 0.1,[16–18] and in patients with cardiorespiratory disease.[19–21] In the range 56–99.5% all studies found good correlation with arterial blood samples with correlation coefficients (r) of 0.82–0.99. The manufacturer's quoted accuracy is approximately within 2% in the 50–100% saturation range. No published data are available for lower saturations but this is not in a clinically useful range. This compares with the accuracy achieved for direct reading oximeters in ideal circumstances of within 3.8%[13] and up to within 4% for a more recent, but nonpulse, oximeter which uses eight transmitted wavelengths and microprocessing.[22]

Sources of error

Pulse oximeters are usually unaffected by skin pigmentation in coloured patients, but raised bilirubin concentration will cause under-reading of the true saturation as it absorbs light in the wavelengths used. The presence of carboxyhaemoglobin will lead to an overestimation of the $S\mathrm{ao}_2$ of the total haemoglobin of blood, but it has recently been shown that the indicated saturation is an accurate reflection of the saturation of the haemoglobin available for oxygen delivery.[23]

Physiology

Apart from technical considerations, the limitations of pulse oximetry are determined by the shape of the oxygen dissociation curve (Fig.3) and oxygen tension is therefore a more clinically useful measurement of blood oxygenation than saturation. Above 94% saturation, corresponding to a $P\mathrm{o}_2$ of 10 kPa, large changes in tension occur with only small changes of saturation, and it is not sensible to relate saturation to $F\mathrm{IO}_2$ or to make deductions about $P\mathrm{ao}_2$. When the $S\mathrm{ao}_2$ has fallen to 83%, the $P\mathrm{ao}_2$ is only 6.65 kPa (50 mmHg), an unacceptably low level. In contrast to the P_{50} it could be called the saturation 50 point (i.e. the saturation at which the $P\mathrm{ao}_2$ is 50 mmHg).

To give an effective warning of impending hypoxaemia in a patient with a normal P_{50}, the instrument must be set to alarm when the $S\mathrm{ao}_2$ falls below 94%. Only hypoxia is detected arising,

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Spinal anaesthesia with hyperbaric lignocaine for elective Caesarean section

M. BEMBRIDGE, ROSEMARY MACDONALD AND G. LYONS

Summary

This study was carried out in 30 patients undergoing elective Caesarean section to assess the predictability and reliability of spinal anaesthesia with 5% hyperbaric lignocaine, with a view to incorporating the technique in our failed intubation drill. The spinal was performed with a 25-gauge needle in either the sitting (15 patients) or left lateral position (15 patients). The speed of onset of anaesthesia to T_6 was significantly faster ($p < 0.01$) in the lateral group, but the duration of action was similar in both groups. Twelve patients had hypotension and four developed severe postspinal headaches. The block progressed to the C_2 dermatome in four patients and was associated with dysphagia. This was totally unpredictable and may be due to altered cerebrospinal fluid dynamics in late pregnancy. Therefore, the use of spinal anaesthesia with heavy lignocaine may be inadvisable in obstetric patients, especially following failed intubation.

Key words

Anaesthetic techniques, regional; spinal.
Anaesthesia; obstetric.

A failed intubation drill is mandatory in every maternity unit.[1] The teaching in this hospital is to initiate the drill early during a difficult intubation and to proceed with epidural anaesthesia.[2] When urgent delivery of the infant is required, the time necessary to establish an adequate epidural block may be too great and spinal anaesthesia with its fast onset has been suggested as being more appropriate.[3] The high blocks obtained with isobaric bupivacaine make it an unsuitable agent in these circumstances[4] and a hyperbaric solution with the potential predictability of spread in the subarachnoid space might be more appropriate.[5]

Lignocaine has several potential advantages, especially in an emergency. It has a rapid onset of action, thus enabling surgery to be started quickly, and a relative short duration of action enabling patients to regain mobility of their legs quickly.[6] The present study was therefore undertaken to evaluate the predictability, acceptability and safety of 5% heavy lignocaine in spinal anaesthesia for elective Caesarean section, with a view to incorporating this technique in our failed intubation drill.

Methods

Thirty patients who requested regional anaes-

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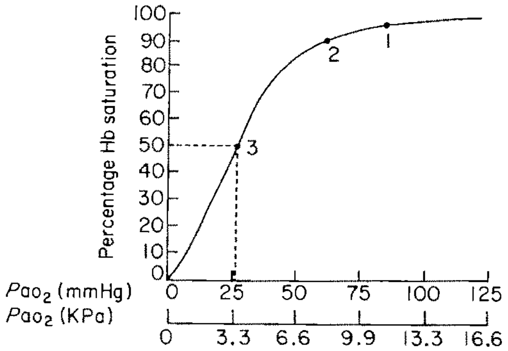

Fig. 3. Normal oxyhaemoglobin dissociation curve. Point 1:94% saturation, $Pa\text{O}_2$ 10 kPa (see text); 2:89% saturation, $Pa\text{O}_2$ 7.7 Kpa; where hypoxia is usually clinically detectable; 3:normal P_{50}.

for example, in conditions of reduced inspired oxygen or minute ventilation or increased oxygen consumption or alveolar–arterial oxygen difference. It is of no value in stagnant, anaemic or histotoxic hypoxia. In certain haemoglobinopathies and diseases, an appreciation of the P_{50} and shape of the oxygen dissociation curve is useful in the clinical interpretation of observed changes of saturation during anaesthesia. In patients with a right shift of the curve, e.g. in sickle cell anaemia, small falls in saturation will be of less significance to tissue oxygenation than patients with a left shift of the curve, e.g. in thalassaemia and after large blood transfusions. Thus, with a normal P_{50} of 3.53 kPa, a $P\text{O}_2$ of 10 kPa corresponds to a saturation of 94%, while in a patient after massive blood transfusion, when the P_{50} may fall to 2.53 kPa, a $P\text{O}_2$ of 10 kPa corresponds to 98% of saturation.[24]

Clinical evaluation of pulse oximetry

Anaesthetic use

A Biox III pulse oximeter (Ohmeda) has undergone evaluation for approximately 8 months. Before proceeding with the clinical evaluation, the accuracy of the instrument was checked by comparing 96 readings of $Sa\text{O}_2$ with the saturation of simultaneously taken arterial blood samples (analysed on a calibrated IL 282 co-oximeter) from 12 patients undergoing anaesthesia or in the intensive care unit. Accuracy in the 75–99.9% $Sa\text{O}_2$ range evaluated was good, with a correlation coefficient (r) of 0.88 ($p < 0.001$) confirming for the test instrument previous reports for this type of apparatus.[18,20]

The presence of cyanosis in the skin or mucous membranes is the only primary obvious clinical manifestation of hypoxia and is an invaluable sign in anaesthesia. In anaemia, conditions of venous stasis or poor peripheral perfusion its presence or absence may be an unreliable indicator of hypoxia. Ambient lighting may have a considerable effect on the detection of cyanosis and even when all conditions are optimal,[23] it can only be reliably detected in the buccal mucosa and lips (but not earlobes and nail beds) when the saturation has fallen to, on average, 89% (Fig. 3). In many situations during anaesthesia, conditions are not optimal: poor or dimmed lighting, obscuring surgical drapes, the patient's position together with limited access to skin and mucous membranes are all common. It is during such cases and in procedures where it is known that hypoxia may commonly occur, that we found the pulse oximeter to be especially useful. (Table 1; Fig. 4).

Using a pulse oximeter as a continuous monitor throughout the peri-operative period, we found that most periods of reduced $Sa\text{O}_2$ occur during the induction or recovery phases, from preventable causes. The early recognition of hypoxia allows appropriate action to be taken and we found the pulse oximeter to be a useful training and teaching aid.

The changes in $Sa\text{O}_2$ were recorded in 45

Table 1. Uses of pulse oximetry

Anaesthesia
- Routine peri-operative monitoring
- Specific advantages with:
  - Reduced lighting, e.g. endoscopy, angiography
  - Reduced skin and mucous membrane access, e.g. ENT, neurosurgery
  - Altered skin circulation, e.g. head down position
  - Increased pigmentation, e.g. coloured patients, post-lymphangiogram
  - Procedures with known risk of hypoxia, e.g. one lung anaesthesia, bronchoscopy
  - Patients with known pre-operative hypoxia
- Training of anaesthetists

Intensive care
- Monitoring oxygenation during procedures, e.g. physiotherapy
- Respiratory failure, IPPV and weaning
- Staff education

Other uses
- Respiratory function tests
- Pre-operative assessment
- Sleep apnoea studies
- Angiography, cardiac shunt studies, etc

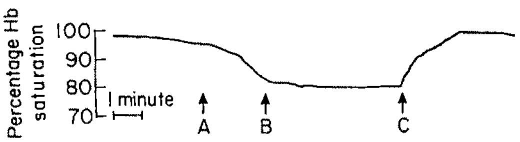

Fig. 4. Changes in $S\mathrm{aO}_2$ during one-lung anaesthesia. A 66-year-old woman undergoing open lung biopsy of left lower lobe lesion; mild restrictive pattern lung function tests. Anaesthesia: thiopentone, pancuronium, fentanyl, N_2O, O_2 ± halothane via Robertshaw double-lumen tube. A: Change to one-lung anaesthesia. $F\mathrm{IO}_2$ 0.5, $S\mathrm{aO}_2$ 95% $P\mathrm{aO}_2$ 13.8 kPa; B: rapid fall in $S\mathrm{aO}_2$: $F\mathrm{IO}_2$ changed to 1.0; C: $S\mathrm{aO}_2$ continues to fall. $P\mathrm{aO}_2$ 7.0. On basis of oximeter reading revert to two-lung anaesthesia. Operation continued satisfactorily using lung retraction without hypoxia on $F\mathrm{IO}_2$ 0.5.

patients during induction of anaesthesia for elective surgery. The patients were selected at random and were anaesthetised by several anaesthetists who had a minimum of 9 months' experience. The anaesthetists were unaware of the purpose of the study and could not see the oximeter display. The anaesthetic technique was not influenced by the presence of the observer, all patients received an intravenous induction and none were pre-oxygenated. The maximum fall in $S\mathrm{aO}_2$ was recorded.

The results are shown in Table 2. Patients were classified and divided according to the ASA system into two groups: ASA 1, ASA 2, 3. The majority of the latter group had cardiovascular disease and were significantly older than the other group, although the pre-induction $S\mathrm{aO}_2$ was the same. Small transient decreases in oxygen saturation during induction are of little significance, but decreases of 5% or more may take the patient into the hypoxic range, which may be important in the presence of pre-existing disease. Our results show that such reductions occurred significantly more frequently in the ASA 2 and 3 group of patients and demonstrates the desirability of pre-oxygenation of patients prior to induction of anaesthesia, especially in those with reduced cardiorespiratory reserve. In a second study, pre-oxygenation of 80 ASA 1 patients effectively eliminated falls in saturation during induction of anaesthesia with a new intravenous anaesthetic agent (propofol) and thiopentone, despite the occurrence of some prolonged apnoeas.[26]

Table 2. Changes in $S\mathrm{aO}_2$ observed on induction of anaesthesia

	ASA 1	ASA 2 and 3
n	30	15
Male:female	6:24	3:12
Age (years, SEM)	36.3 (2.77)	50.6* (6.06)
Pre-induction $S\mathrm{aO}_2$ (SEM)	97.3 (.291)	97.2 (0.49)
Decrease in $S\mathrm{aO}_2$ during induction		
0†	3 (10%)	2 (13%)
1–4%	20 (60%)	4 (26%)
5–9%	7 (23%)	6† (40%)
10+ %	0	3† (20%)

*t-test $p<0.05$.
†Chi squared $p<0.05$ (saturation falls >5%).

The pulse oximeter works well during pulsatile flow cardiopulmonary bypass (Fig. 5) and using the ear probe we found it was rarely affected by poor peripheral perfusion due to hypothermia or the administration of inotropes. However, some transient interference from diathermy does occur.

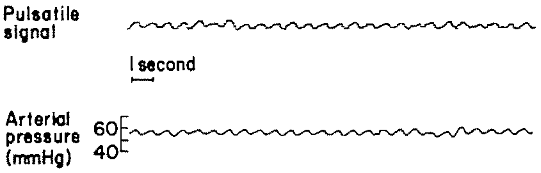

Fig. 5. Pulse oximetry during pulsatile flow cardiopulmonary bypass at 25°C, using ear probe. The diagram shows pulsatile output from oximeter compared with left radial artery pressure trace. The $S\mathrm{aO}_2$ reading was 98% and was accurate when compared with arterial blood gas analysis using an IL 282 co-oximeter.

Use in the intensive care unit. The majority of patients treated for respiratory failure in the intensive care unit will have invasive cardiovascular monitoring, but the adequacy of pulmonary gas exchange is usually only intermittently assessed by arterial blood gas analysis. Such patients are at risk of developing acute hypoxic episodes during suction, physiotherapy and weaning, and in some lung pathologies, e.g. pulmonary haemorrhage, sudden desaturation may occur.

Physiotherapy in the form of postural drainage, percussion–inflation and simulated cough with bag-squeezing[27] is required by many patients receiving intensive care whose tracheas are intubated. These manoeuvres may be associated with hypoxia, a reduction of cardiac output[28] and dysrhythmias, and some form of continuous oxygen monitoring is desirable. We have evaluated the Biox III during these procedures. The finger probe is unsatisfactory as it tends to fall off as the patient is moved, but the ear probe is satisfactory, especially if the head band provided is used. The pulse oximeter rapidly

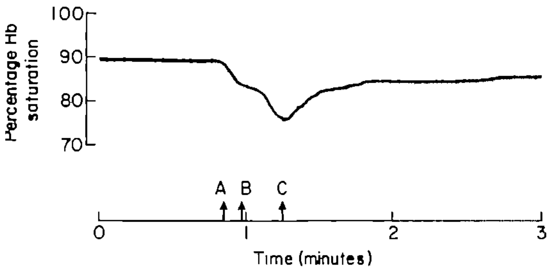

Fig. 6. Saturation changes observed during tracheal suction. An intubated intensive care patient who was weaning from IPPV and breathing humidified oxygen, $F\text{IO}_2$ 0.4 spontaneously. A:nurse disconnects patient from breathing system without pre-oxygenation; B: unnecessary delay before start of suctioning at point B; C: maximum fall in saturation. Over 3.5 minutes elapsed before $P\text{aO}_2$ rose to levels before suction.

detects falls of $S\text{aO}_2$ and the alarm alerts attendant staff. In this and other usage, apart from clinical monitoring, the oximeter has potential for staff education and training (Fig. 6).

Other uses. The pulse oximeter has other applications, e.g. during respiratory function tests,[29,30] pre-operative assessment and sleep apnoea studies. We have found it particularly useful in the diagnosis and treatment of some rare disorders, such as during embolisation of pulmonary A-V fistulas, and we regard it as mandatory when setting up new experimental techniques of ventilation (high frequency ventilation, oscillation and continuous flow ventilation).

Conclusions

There is a definite need for a simple, accurate, noninvasive way of continuously assessing the arterial oxygenation of blood during anaesthesia, as patients still die or are damaged due to the delayed detection of hypoxia. The development of new and often complex apparatus for the administration of anaesthesia and their use in intensive care increases this need. Similarly, the oximeter can be useful during the setting up procedures of new forms of ventilation, for example high frequency ventilation and oscillation, and in the intensive care patient in situations and clinical conditions where rapid changes of oxygenation may occur.

The cost of pulse oximeters is high at present, but this is similar to transcutaneous $P\text{O}_2$ electrodes, which are less suitable for anaesthetic use and also have high running costs.[31]

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Anaesthesia, 1986, Volume 41, pages 950–960

SPECIAL ARTICLE

In pursuit of relaxation*

J. P. PAYNE

Summary

This is an account of personal research which spans nearly thirty years.

Key words

History; curare.
Neuromuscular relaxants; suxamethonium, decamethonium, atracurium and vecuronium.

The introduction of curare into clinical anaesthesia in 1942 by the late Harold Griffith[1] and his young colleague Enid Johnson was one of the most significant advances ever made in the specialty and, almost overnight, changed the whole concept of anaesthetic practice. The modern story of curare in anaesthesia began, incongruously enough, in 1934 when Richard Gill, a young eccentric adventurer and explorer, returned to Washington DC, USA from the jungles of South America stricken by some form of spastic paralysis. The diagnosis of multiple sclerosis, made by the neurologist called to see him appalled Gill who, as a former student of medicine, was fully aware of its significance. In his despair the chance remark by his doctor that what he needed to relax his spasms was a drug like the arrow poison used by South American Indians established in Gill a new sense of purpose. Despite his spastic state he laboriously taught himself to walk again and 4 years later he hobbled back into the jungle in pursuit of the drug that would give him relaxation. When he returned to the United States, he had with him 25 lb of the raw curare which he eventually sold to the pharmaceutical company E.R. Squibbs and Sons; this company produced the first commercial preparation of curare under the trade name of Intocostrin. Initially it was used only by psychiatrists to control the drug-induced convulsions which formed part of the treatment of certain psychotic states. However, one physician in the company, Dr Lewis Wright, believed that the drug had potential value in anaesthesia and canvassed his ideas amongst the leading anaesthesiologists in North America. Few were interested and most ridiculed the whole idea; even those who were sufficiently receptive to undertake animal work were not prepared to use the drug in man.[2]

That was the situation in 1941 when Dr Wright attended an anaesthetic conference in Montreal and met up with his old friend Dr Harold Griffith, a local anaesthesiologist, who enquired about the progress of curare. Dr Wright had to confess that he had been unable to find a clinician willing to test the drug whereupon Griffith volunteered to

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*Based on a Hunterian Lecture delivered on 23 January 1985 at the Royal College of Surgeons of England.

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undertake the task if Dr Wright would supply him with it. Griffith studied the various reports that accompanied the supply of Intocostrin and became convinced that no further animal work was necessary. Either it would work on patients, or it would not, and there was only one way to find out. There is no better example of the application of John Hunter's famous injunction to Edward Jenner 'But why think, why not try the experiment'. Harold Griffith tried the experiment and the rest is history.

Those anaesthetists who began their training in anaesthesia after the introduction of the neuromuscular blocking drugs can have little understanding of the anaesthetic routines before that time. Until then a rapid smooth induction of anaesthesia and the maintenance of a steady state adequate for the surgical procedure was a work of art accomplished regularly by relatively few and then only after years of diligent practice.[3] This is true no longer. Unconsciousness can, at best, be produced rapidly by the intravenous injection of a barbiturate or some other rapidly acting hypnotic and profound muscular relaxation can be induced almost immediately thereafter by the use of a blocking agent. The patient is, at worst, at the mercy of any doctor, however unskilled, who can manage to put a needle into a vein.

Importance of John Hunter

On first consideration it might be thought that with a time interval of more than 150 years, John Hunter could have little to contribute to modern anaesthetic practice yet in his 'Proposals for the recovery of people apparently drowned'[4] he made at least two observations that are still relevant. Hunter was well aware from his experiments on dogs that once the breathing had stopped, artificial ventilation was necessary to keep the animals alive and he reasoned that a similar method would be effective in man. To this end he set about designing what was in effect the first positive pressure ventilator with a negative phase. He constructed, 'a pair of bellows so contrived with two separate cavities that by expanding them when applied to the nostrils or mouth of a patient one cavity may be filled with the common air, and the other with air sucked from the lungs; and by shutting them again, the common air may be thrown into the lungs, and that which is sucked out of the lungs be discharged into the room'.

Had a similar awareness of the need for ventilation been shown by those anaesthetists who first used curare, much of the early morbidity and even mortality would have been avoided. Initially attributed to an inherent toxicity, especially by anaesthetists in North America, it was only later that these complications came to be recognised as the consequences of underventilation.

The second of John Hunter's comments that has particular relevance to the use of neuromuscular blocking agents was his advocacy of the need for cricoid pressure during artificial ventilation. As Hunter pointed out, 'If during the operation of the bellows, the larynx be gently pressed against the oesophagus and spine it will prevent the stomach and intestines being too much distended with air. This pressure however must be conducted with judgement and caution so that the trachea and the aperture into the larynx both be left perfectly free.'

A better understanding of the principles of cricoid pressure among present day anaesthetists could still avoid needless tragedies, particularly in obstetric anaesthesia.

Early neuromuscular relaxants

Within 10 years of the successful introduction of curare into anaesthetic practice, a number of new synthetic compounds had been introduced. They included decamethonium, gallamine and suxamethonium so it soon became obvious that neuromuscular blocking drugs could be separated into two distinct categories, the competitive or non-depolarising agents, as represented by curare and gallamine, and the depolarising drugs such as decamethonium and suxamethonium. However, it also became apparent that the mode of action of both groups of drugs was more complicated than originally thought and even today some of their actions have yet to be explained.

My own involvement in the assessment of neuromuscular blocking drugs arose some 30 years ago when W.D.M. Paton, then Professor of Pharmacology in the Royal College of Surgeons of England, very generously offered me the opportunity to work in his laboratory on a part-time basis. It was a thoroughly stimulating and challenging experience and it is perhaps of interest to reflect that of the little group of research workers directed by Professor Paton at that time, three became professors of pharmacology, two professors of surgery, one a professor of psychiatry and one a professor of anaesthetics. There can be few other basic science departments in the United Kingdom that have had such a widespread clinical influence. For good measure, two of the professors in the team were later knighted, Professor Paton himself and Dr John Vane, who also won the Nobel Prize for Medicine.

When I joined Professor Paton's group my interest was in ganglion blocking and other hypotensive agents and, pharmacologically at least, it was a natural progression into the neuromuscular field in which Professor Paton was so preeminent. A series of experiments in cats demonstrated that the action of these drugs was influenced by such factors as carbon dioxide accumulation, acidosis and alkalosis, of both metabolic and respiratory origin, and the presence of other drugs. It was also shown that those drugs categorised as competitive blocking agents sometimes showed an initial transient stimulant action before signs of block became obvious.[5] Nevertheless, helpful as such animal experiments were, they could not be directly extrapolated to patients and it was therefore decided that an attempt should be made to carry out similar studies in man.

Measurement of neuromuscular effect

At about that time Professor Martin Holmdahl, currently the Rektor Magnificus of the U of Uppsala, was working with me as an lecturer in the Postgraduate Medical S Hammersmith Hospital. Between us we system for recording the evoked singl responses of the small muscles of the anaesthetised patients. We decided that study should be limited to suxame because of its short duration of action further agreed that it would be necessar demonstrate that the repeated injectio drug would produce a consistent effect. failed to do; instead we demonstrated t cessive doses became steadily less effecti in due course, this observation led to detailed examination of the phenom *tachyphylaxis* seen with depolarising dr

Before that could happen it was nece establish a more sensitive approach measurement of the evoked response of In particular, the need to develop quantitative methods of assessment cognised, as was the importance of criteria with an identifiable physiological (Fig. 1). Accordingly, the available te were examined and re-assessed and, as a r developed a method for the quantitative tion of neuromuscular blocking drugs t these requirements. We proposed th accurate assessment of the action of muscular blocking drugs was to be mad it would be necessary to measure single tw

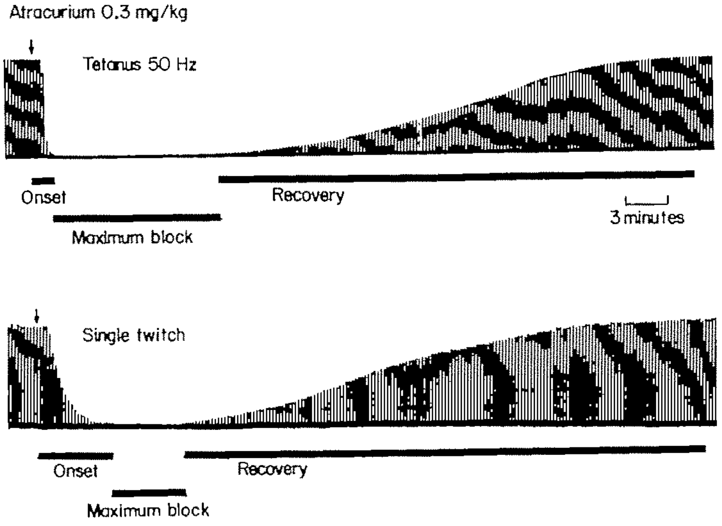

Fig. 1. This illustrates the pattern of the tetanic and single twitch contractions of the adductor pollicis muscles of the hands after injection of a competitive neuromuscular blocking drug.

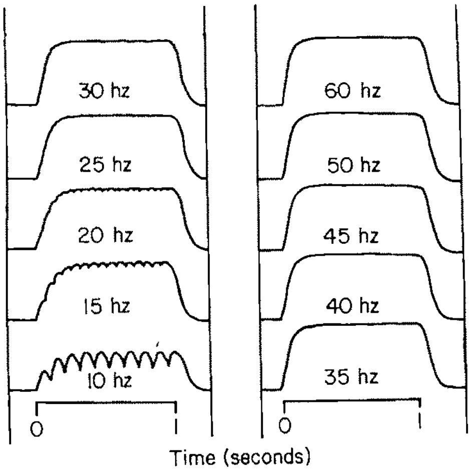

Fig. 2. Response of adductor pollicis muscle to stimulation of corresponding ulnar nerve for 1 second at a series of different frequencies. In this particular experiment the tracings were virtually identical above 40 Hz. (*Journal of Applied Physiology* 1975; **39**: 714–7).

tetanic contractions simultaneously.[7] For this purpose the small muscles of the hand proved to be most suitable, but there was little information available about the ideal tetanic pattern needed. A study was therefore undertaken to determine the pattern of the tetanic force development of the adductor pollicis muscle. It was shown that fusion of the tetanus had usually occurred at a stimulation rate of 40 Hz (Fig. 2), that the mean maximal force was developed at a mean frequency of 75 Hz and that it was well maintained up to a stimulation frequency of 100 Hz. On this basis it was decided to use a frequency of 50 Hz which is still within the physiological range and thus unlikely to cause any significant fatigue.[8]

The advantage of measuring the tetanic contraction is that it provides information not only about the degree of block but also about the extent of fade which many believe is a presynaptic phenomenon.[9] Moreover, there is evidence that the pattern of fade differs from one drug to another and the possibility that each drug has a specific profile needs to be explored more thoroughly.[10]

The subsequent studies were carried out on volunteer patients about to undergo elective urological surgery and from whom informed consent had been obtained. Simultaneous measurements of tetanic and single twitch contractions of the adductor pollicis muscles were made by means of two force transducers mounted, one in each hand, to record the force of the thumb adduction. For this purpose, appropriate Statham force transducers incorporated in suitable handgrips were used. Each ulnar nerve was stimulated supramaximally through subcutaneous needle electrodes implanted at the wrist by means of a stimulator fitted with an isolation unit and a digitimer. The tetanic stimulus was produced through a gated pulse generator. One ulnar nerve was stimulated every 12 seconds with tetanic bursts of 50 Hz for one second. The other was stimulated by a single square-wave pulse of 200 ms duration repeated at 12-second intervals. The contractions were recorded simultaneously at two different speeds, 5 mm/minute and 5 mm/second. The arterial blood pressure was measured directly from a polyethylene catheter inserted into a radial artery at the wrist. Together with the electrocardiogram, it was recorded continuously throughout the procedure.[11]

The techniques just described were used to investigate the effects of suxamethonium on the tetanic contractions of the adductor pollicis muscle and to compare these effects with those on the corresponding twitch responses.[7] In most patients, a dose of 0.2 mg/kg completely blocked the tetanic response but only partially blocked the twitch, which also recovered more rapidly than the tetanic response. Two related observations were of particular interest; first, a substantial degree of overshoot was seen at the end of the recovery of the twitch which was not present when the tetanus recovered and, second, a degree of fade directly related to the frequency of stimulation was seen after every injection of suxamethonium.

Fade, tachyphylaxis and suxamethonium

On the basis of these results it was decided to extend the earlier work of Payne and Holmdahl[6] who demonstrated the onset of tachyphylaxis when suxamethonium was given repeatedly in small doses to anaesthetised man. Suxamethonium 0.2 mg/kg was given repeatedly at 15-minute intervals. In the case of the single twitch, tachyphylaxis developed rapidly but the tetanic contractions showed an increasingly prolonged recovery time. Thus, suxamethonium given in this way produced a response that differed both quantitatively and qualitatively when the tetanus was compared with the twitch. When the phenomenon of tachyphylaxis was explored in more detail, it was demonstrated that, whereas initially the anticholinesterase agent edrophonium enhanced both the tetanic and the twitch response to suxamethonium, the enhancement was gradually reduced with succeeding doses and ultimately an antagonism developed similar to that seen when edrophonium was given in the presence of competitive blocking drugs[11] (Fig. 3).

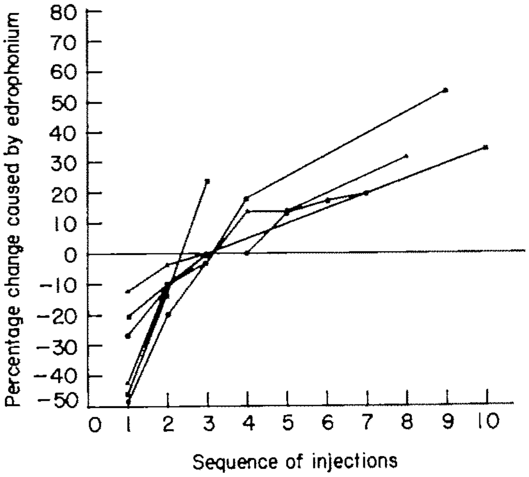

Fig. 3. Alteration in the % change of tetanic contractions produced by edrophonium (0.1 mg/kg) in six patients during repeated administration of suxamethonium (0.2 mg/kg) every 15 minutes. (*British Journal of Clinical Pharmacology* 1975; **2:** 487–94.)

The possibility that the qualitative and quantitative differences between the tetanic and single twitch responses seen in the presence of suxamethonium could also be demonstrated with competitive blocking agents needed to be considered. For obvious reasons it was not practicable to use the repeated dose technique so successfully employed with suxamethonium and it was decided, therefore, to examine any possible interaction with an inhalation agent like halothane. Accordingly, patients were exposed to concentrations of 1% and 2% halothane for 10 minutes during recovery from neuromuscular block by tubocurarine, dimethyl tubocurarine and gallamine. During the exposure to halothane the peak height of the tetanic contraction was gradually reduced with time and, simultaneously, the tetanic fade was increased; the single twitch response was unaffected and continued to recover as before. When the halothane was withdrawn, the peak height immediately began to recover and a similar pattern was seen with the fade.[12]

Neostigmine

To explore the nature of this partial block, other patients were given intravenous neostigmine during partial block with the same competitive blocking agents in the presence of 2% halothane. In the nine patients studied, intravenous neostigmine in a dose of 2.5 mg preceded by atropine 1.2 mg invariably restored normal transmission, so that it can be reasonably assumed that the block was essentially competitive. However, when a second dose of neostigmine was given 2–3 minutes later, the block was re-established. It was obviously important to know whether this was a phenomenon related to the presence of halothane or whether it could occur in its absence. The relevant study was carried out under the same conditions, but without the presence of halothane and exactly similar effects with neostigmine were demonstrated.[13]

A possible explanation for this effect was that the tetanus had fully recovered from the block after the first dose of neostigmine so that the second was acting on normal unblocked motor endplates. To test the validity of this hypothesis, a group of patients who had not been given neuromuscular blocking drugs were studied. Each patient received either two or three intravenous injections of 2.5 mg neostigmine after pretreatment with atropine 1.2 mg by the same route. In each patient the peak height of the tetanus was substantially diminished and this was associated with a marked degree of fade. The single twitch was either not affected or slightly enhanced. Moreover, what was equally interesting was that when a small dose of intravenous gallamine (10 mg) was given to four of these patients when the block had reached its maximum, the peak height was restored to normal and the fade was abolished (Fig. 4). Under the circumstances, it seemed reasonable to test the corollary and, accordingly, once neostigmine block had been established, a small dose of suxamethonium (0.3 mg/kg) was given intravenously and, as expected, substantially enhanced and prolonged the block.[13]

The clinical significance of block by neo-

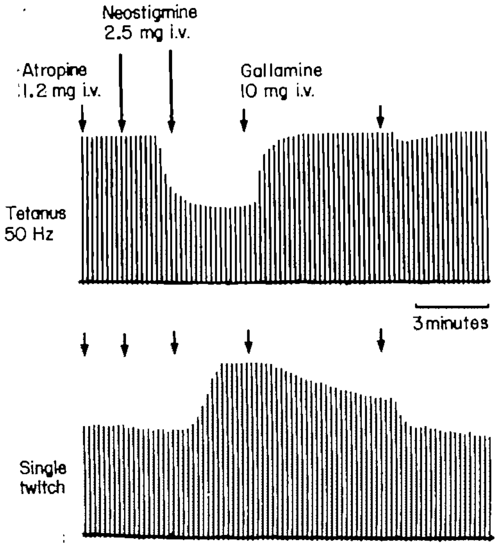

Fig. 4. Tracings from an anaesthetised patient, showing neuromuscular block of the tetanic response after two doses of neostigmine 2.5 mg, preceded by atropine 1.2 mg, and the potentiation of the single twitch. Gallamine 10 mg antagonised the neuromuscular block of the tetanic response and reversed the potentiation of the single twitch. (*British Journal of Anaesthesia* 1980; **52:** 69–76.)

stigmine should not be underestimated. These results have demonstrated conclusively that neostigmine in doses commonly used clinically is capable of producing a depolarising type of block that can be enhanced and prolonged by suxamethonium. Anecdotal accounts of neostigmine-resistant curarisation abound, particularly in relation to patients in recovery wards and intensive care units, although the hard evidence on which the diagnosis is based is weak and hard to find. I would like to suggest that such block is not neostigmine-resistant but neostigmine-induced.

Decamethonium

For the sake of completeness we decided to study the related properties of decamethonium, the only other depolarising blocking drug to have been used clinically.[14] Chemically, it is the simplest of all neuromuscular blocking drugs and it can also be regarded as a clean drug; that is to say, its action is highly specific and it is not metabolised into a series of breakdown products that have separate and significant pharmacological actions.

The drug was given in divided doses to nine anaesthetised patients and the total dose was repeated two to three times once complete recovery from block had been obtained. Tachyphylaxis was demonstrated after the second or third series of injections; the tetanic response was more affected than that of the single twitch and its pattern was more consistent. In effect, at least twice the total dose was needed with subsequent injections to obtain the same results as with the first series of injections. If the subsequent injections were restricted to the same amount as in the first series, the degree of block was substantially reduced. If the patient was exposed to halothane during recovery from the first series of injections, no blocking effect of halothane was seen. If, however, exposure occurred after the development of tachyphylaxis, the neuromuscular block was enhanced. The reverse was true with neostigmine. When the drug was given during recovery from the first exposure to decamethonium the block was enhanced, but when neostigmine was given during partial block, after tachyphylaxis had been established, the block was antagonised. Thus, the neuromuscular blocking action of decamethonium, like that of suxamethonium, changes after repeated dosage and comes to resemble that of the competitive neuromuscular blocking agents.[15]

New drugs

Despite the immediate success of curare in anaesthetic practice its properties are not ideal. In particular, its lack of specificity sometimes produced problems, for example when it was used in asthmatic patients. It was not long, therefore, before chemists, pharmacologists and anaesthetists began the search for a more suitable drug, free from the disadvantages of curare. That search is still continuing; despite the quality of some of the new synthetic compounds, the ideal neuromuscular blocking agent has not yet been found.

Two promising new compounds have been made available in the United Kingdom within the last few years. These are atracurium and vecuronium.

Atracurium

Atracurium was designed specifically to take advantage of the well known Hofmann elimination pathway, whereby the drug can be broken down in the blood at a pH and temperature within the physiological range and without the need to rely on hepatic or renal elimination.[16] The pharmacological properties of atracurium were tested at the Wellcome Research Laboratories Beckenham by Hughes and Chapple,[17,18] who showed that the drug was a powerful competitive neuromuscular blocking agent in a wide range of laboratory animals and that it was free from any significant side effects. Accordingly, atracurium was selected for further study in man. The Research Department of Anaesthetics undertook this task and it was first used clinically in St Peter's Hospital, Covent Garden, early in 1979. Later in the year, a preliminary report of our findings was presented to the Anaesthetic Research Society at the winter meeting at the London Hospital.[19]

The intravenous dose of atracurium was restricted at first to 0.2 mg/kg. The tetanic response was almost completely abolished but the twitch was more resistant; only about 75% block was achieved with this dose. When the dose was increased to 0.3 mg/kg, tetanic block was complete and the twitch was only just present. The difference in sensitivity between the two responses ceased to be significant at doses above this level. As the dose of atracurium was increased to 0.6 mg/kg, the speed of onset of maximum block became faster, but at all times maximum block of the tetanic response preceded that of the twitch. At doses above 0.6 mg/kg, no further change in the speed of onset was seen and it was decided therefore to recommend a dose level up to 0.6 mg/kg for use in man.[20]

This was a correct assessment for purely scientific reasons but, in retrospect, it might have been better for clinical purposes to have recommended a dose of 0.5 mg/kg. The difference in effect between the two doses is minimal and most people find the latter easier to calculate.[21]

The process of recovery was equally interesting. The twitch response returned to normal faster than the tetanus, the two components of which, the peak height of the contraction and the sustained contraction, recovered at different rates. Initially, the tetanic response resembled that of a single twitch in that a certain height was reached, but the tetanus was not sustained. The fade began to disappear as the recovery process continued, so that ultimately the initial peak height was overtaken by the sustained response into which it became fused. When the recovery of the peak height after atracurium was compared with that after equivalent amounts of other established neuromuscular blocking drugs, it could be shown that the recovery after atracurium was faster (Fig. 5). Similarly, the sustained tetanus recovered more rapidly after atracurium than after the administration of these drugs. The failure to sustain a tetanus in the presence of neuromuscular blocking drugs has been attributed to a presynaptic action of the drugs, whereby the output of acetylcholine is reduced.[22] The fact that different neuromuscular blocking drugs have different recovery profiles suggests that the degree of suppression is not uniform.

It has been suggested that the train-of-four response, originally introduced by Roberts and Wilson[23] in Liverpool, to assess the state of muscles in myasthenia gravis, would exhibit the same degree of sensitivity to the presence of fade as demonstrated by the tetanic response. However, when neostigmine was used to produce partial block in a patient who had just recovered from the atracurium block, train-of-four stimulation failed to detect the existence of fade although it was clearly apparent in the tetanic response[24] (Fig. 6).

A particular advantage of atracurium in the management of anaesthesia is the predictability of the response to a divided dose technique, which implies a lack of cumulative effects within the dose regimen chosen.[25,26] Normally, the first dose will produce adequate relaxation for 20–40 minutes, but once recovery has begun spontaneous breathing returns early and rapidly within a few minutes of the re-appearance of the tetanic response.[27] This rapid recovery discomfited some anaesthetists who have complained that unless a careful watch is kept on the patient, the rapid return of muscle activity could embarrass the surgeon and themselves. However, since the purpose of their employment is to care for the patient, such criticism is scarcely valid. It could equally be regarded as criticism of the professional standards of the individuals concerned.

The reproducibility of the effects of atracurium and its relatively short duration of action offered the opportunity to study the pharmacokinetic and pharmacodynamic pattern of the drug. Anaesthetists tend to fight shy of any involvement in such matters, largely because they have

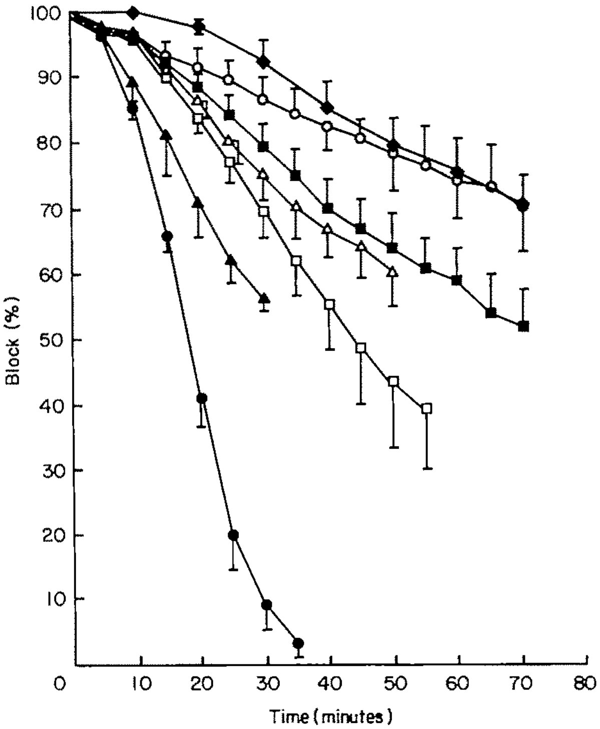

Fig. 5. The graph showing that the peak height of the tetanic contraction recovers faster after block with atracurium than after block with other established competitive blocking agents. Mean (SEM). ●, Atracurium, $n = 5$, 0.2 mg/kg; ▲, gallamine, $n = 3$, 1.0–1.5 mg/kg; □, fazadinium, $n = 6$, 0.4–0.8 mg/kg; △, Pancuronium, $n = 5$, 0.05–0.06 mg/kg; ■, tubocurarine, $n = 6$, 0.2–0.5 mg/kg; ○, dimethyl tubocurarine, $n = 6$, 0.1–0.3 mg/kg; ◆, alcuronium, $n = 6$, 0.2 mg/kg. All drugs administered intravenously.

been brainwashed into accepting that such complex phenomena are matters for specialist consideration. This is unfortunate because the anaesthetist is better placed than most to carry out such studies. Unlike most clinicians, who merely prescribe drugs and who may not see the patient again for several days or sometimes even for weeks, the anaesthetist prescribes drugs, administers them personally and stays with the patient until the effects have worn off. If it is remembered that pharmacokinetics merely describes what the body does with the drugs and pharmacodynamics defines the effect of drugs on the body, the situation can be brought into perspective.

On this basis the relationship between the kinetic distribution of atracurium and its dynamic effects on the body were investigated in a series of simple studies. Three different methods of dosage were employed. These involved the use of single bolus injections, continuous intravenous infusions and a divided dose technique similar to that commonly used in animal studies.[28] The divided dose technique was employed to establish a dose–response relationship for both tetanic and single twitch contractions. For this purpose, a relatively small dose of atracurium (0.05 mg/kg) was given and the responses to single twitch and tetanic stimuli were measured. Thereafter, the dose was repeated at 3-minute intervals until approximately 95% block of the twitch response had been obtained. The resultant curves emphasised not only the greater sensitivity of the tetanus to block, but also demonstrated a different pattern of onset between twitch and tetanic block.

In the case of the single bolus injections, the height of the tetanic and single twitch contrac-

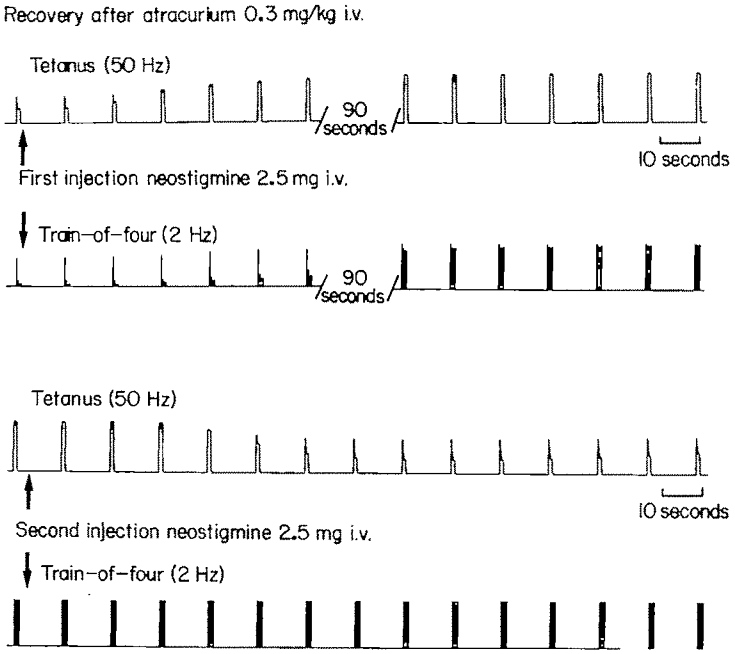

Fig. 6. Traces illustrating the onset of tetanic fade after the injection of a second dose of neostigmine and the inability of the train-of-four to detect it.

tions were measured at regular intervals from the beginning of recovery until it was complete. Blood samples were taken at the same time and spun down to enable plasma concentrations of the drug to be obtained by high performance liquid chromatography (HPLC).[29] The values thus measured were plotted against the corresponding muscle responses after the plasma concentrations had been normalised to a dose equivalent to 1 mg/kg. This was done in order to display the results compactly. A similar approach was adopted in the case of the continuous intravenous infusions which were given for either 30 or 60 minutes in a dose which ranged from 0.002 mg to 0.01 mg/kg. The data obtained were used by Dr Williams and his colleagues to derive a combined kinetic dynamic model which can be used to predict the profile with time of either the tetanic or single twitch response for any regimen of atracurium.[30] Detailed accounts of the development and clinical application of atracurium were presented in 1982.[31]

Vecuronium

More recently, we have had the opportunity to investigate the action of vecuronium, an analogue of pancuronium[32] and with a similar dura action to atracurium. Studies have been using the single bolus,[33] the divided dose continuous infusion techniques (Fig. 7). I early to draw definite conclusions, but the e suggests that there is no great difference b the effects of vecuronium and atracurium single twitch; the tetanic response needs examined in more detail.

Future problems

It is clear that the problems associated w response to neuromuscular blocking drugs from resolved. Indeed, such work as described has raised new problems that will given to me to resolve. Included among th the pattern of tetanic fatigue and the relati between peak height and sustained contr The nature of fade needs study, as dc occurrence of overshoot when the single response has recovered completely and th titative differences between the single twit the tetanus are not yet understood. It may that it will be necessary to return to the laboratory and even to the isolated prep before answers are obtained.

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A matter of vigilance

This is a further comment on Dr Green's Editorial (*Anaesthesia* 1986; **41:** 129–30).

Training of paramedical anaesthetic assistants in this country is not to Scandinavian or American standards, but we do not expect them to administer anaesthetics as Scandinavian practitioners, for example, do. The level of training in this country teaches our assistants to observe the patient and report changes. Does this training, and the fact that this observation is the usual reasonable practice in this country, set a medicolegal standard rather than the use of practices for other countries?

Dr Green is not consistently clear as to how far 'out of theatre' is. Surely any trip from the operating room itself and away from immediate visual contact with the patient and his monitoring devices is too far without leaving a competent observer in place? Would that staffing levels allowed occasional forays into the

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recovery room to oversee previous patients, or to the anaesthetic room to see the next patient, with adequate experienced observation left in the theatre.

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Essex

A reply

Thank you for sending me Dr Eames' comments on my Editorial. Paramedical anaesthetic assistants in the United Kingdom are trained to look after anaesthetic equipment and to observe the progress of an anaesthetic in so far as his help may be required by the anaesthetist at any time. He is not trained to be, nor in my opinion should he be allowed to be, in sole charge of a patient under anaesthesia for any period of time, except in the occasional 'life or death' emergency which takes the anaesthetist away from his patient. Our medicolegal standards require an anaesthetist to be with his patient at all times, whilst an anaesthetic is in progress.

Unfortunately, our busy operating practices do not always allow for the highest possible standards at all times since, unlike airline pilots, we are frequently expected to operate without a trained medical assistant and therefore very occasionally we are forced to take a calculated risk by leaving the theatre to save the life of a patient in recovery. What is totally unacceptable is the practice of leaving patients in order to answer the telephone or to have a cup of coffee. If trained anaesthetists occasionally fail to recognise disconnexions, how can a paramedical assistant be expected to do so?

The distance an anaesthetist goes out of the theatre, during an anaesthetic is, of course irrelevant. Minute-to-minute observations of all physiological variables by a trained observer are vital for maximum safety during anaesthesia; any failure in this discipline is putting the patient at risk.

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Adverse reactions to drugs

The Editorial in the April issue (*Anaesthesia* 1986; **41:** 351–2) and the report of the Annual Linkman Conference (*Anaesthesia* 1985; **41:** 466) failed to point out another cause for under reporting, namely, the difficulty in assessing which drug is an often complex induction sequence is responsible for the reaction.

It is common for more than one intravenous agent to be used at induction; indeed, it may be more correct to say that it is unusual for only one drug to be used. It is seldom practicable to wait to see if a reaction occurs before administering the next drug; although this may be counsel of perfection, one needs to bow to expediency. Nor is it right to assume that the more likely drug is responsible. We reported three cases of reaction to induction agent.[1] Althesin was administered to all three patients, but pancuronium was implicated in one only after skin testing. At this time Althesin was already becoming known as a potent producer of reactions, but pancuronium was thought not to do so.

It may therefore be that uncertainty about the causative agent dissuades the user from reporting.

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Reference

1. TWEEDIE DG, ORDISH PM. Reactions to intravenous agents Althesin and pancuronium. *British Journal of Anaesthesia* 1974; **46:** 244.

A reply

Dr Tweedie has raised a most relevant and important point which is probably of more relevance to anaesthetists than to any other medical specialty. It is even possible that two drugs may interact to cause a severe reaction. Nevertheless, it is important that reactions involving more than one drug be reported. Suspicion will be raised if there are repeated reports involving a particular drug combination. Furthermore, with the present yellow cards we are not asked to attempt to identify the causative agent.

Thank you for pointing out this important omission.

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Oximetry

In their evaluation of the Nellcor pulse oximeter (*Anaesthesia* 1986; **40:** 302–5) Dr Tytler and Dr Seeley make reference to my review of oxygenation monitoring,[1] but conclude that oximetry is unlikely to become a routine technique during anaesthesia, except where hypoxaemia may be expected. This conclusion would be reasonable if the anaesthetist could readily detect hypoxaemia. However, all the evidence suggests that this is not the case. Cyanosis is not detected until hypoxaemia is profound[2] and many intra-operative hypoxaemic events are only noticed when secondary changes such as bradycardia occur.[3] Our own experience with oximetry over the past 3 years confirms the difficulty of detecting hypoxaemia by clinical means. Professor Gray, in a recent review of anaesthetic mishaps,[4] lists six maxims for safe anaesthesia. Four of these six common errors of judgement involve hypoxaemia.

Monitoring of oxygenation during routine anaesthesia is necessary because not only is hypoxaemia difficult to detect, but it is also *unexpected*. Pulse oximeters are, at present, the most practical means for routine monitoring. It would be regrettable if we were forced into the use of such instruments by threat of litigation, as is happening in the United States. Eternal vigilance is only possible when the warning signs are visible or palpable. When they are not, then instruments that extend our senses are not just optional extras but essential.

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The article by Tytler and Seeley concerning pulse oximetry (*Anaesthesia* 1986; **41**: 302–5) should provoke great interest and circumspection amongst anaesthetists on this side of the Atlantic. However, I must say that I find their conclusion that 'the adoption of this technique during routine anaesthesia seems unlikely in the United Kingdom' to be extremely depressing. No single form of monitoring is so apposite to the practice of anaesthesia. In one simple piece of noninvasive apparatus one has reliable monitoring during induction and maintenance of anaesthesia of oxygen saturation, perfusion and pulse rate. The implications for its use in recovery need hardly be stated. Indeed, it should become routine to prescribe pulse oximetry postoperatively, just as one does oxygen at present.

What is the objection to this great advance in monitoring? Conventional anaesthetists will undoubtedly state that it is unnecessary and one should rely on clinical signs. Did we not hear the same arguments about electrocardiographic monitoring, oxygen and pressure alarms, peripheral nerve stimulators, automatic oscillometric blood pressure machines and so on? Pulse oximetry represents a much greater advance than any other form of monitoring presently available and will thus make the greatest contribution to patient safety. No, the obvious objection must be cost. One has to admit that the original machines at £6000 were just too expensive to be able to justify routinely. However, machines are now available for half this price.

Those of us who have used these machines routinely need no persuading. Those of us in departments who have had hypoxic disasters in the recovery room should need none either. Those hospitals who are having to pay the cost for such disasters may feel that routine provision of this equipment is 'cheap at the price'. If anaesthetists agree with my contention, then we must, as a group, insist that these machines become routinely available and also insist that they are used. It might even result in further price reductions!

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A reply

Thank you for the opportunity to reply. We agree with all the points that Dr Hanning and Dr Green raise. It is unfortunate that the statement in our article, that pulse oximetry is unlikely to be adopted during routine anaesthesia in the United Kingdom, has been misunderstood. Our belief is based neither on the evaluation of the Nellcor instrument nor on the usefulness of the technique; we agree that pulse oximetry is an outstanding advance in monitoring. It is, alas, based on bitter experience of the financial problems facing the National Health Service and the reluctance of some anaesthetists to make use of monitoring which is already available.

Our statement was not a conclusion but a prediction. We should be delighted if we were to be proved wrong.

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Anaesthesia and plasma cholinesterase deficiency

The account of Drs Morrison, Robinson and Macleod (*Anaesthesia* 1986; **41:** 323–4) of their management of anaesthesia for emergency Caesarean section in a patient with known plasma cholinesterase deficiency was interesting.

They state that although they would normally have managed this problem with a regional technique, they deemed a general anaesthetic mandatory on the basis of speed. In this sort of situation the mother's safety is of paramount importance and a spinal anaesthetic would have been less hazardous and probably just as quick.

The authors state that suxamethonium is contraindicated since the resultant paralysis would make a failed intubation drill impossible, but how would they have coped if they had failed to intubate the patient, as they chose instead to give her 0.7 mg/kg of atracurium?

Many anaesthetists do not consider the option of a regional technique, where there is a risk of sudden blood loss as here in a Caesarian section for placenta praevia, but with attention to meticulous resuscitation, the use of spinal anaesthesia would, in my opinion, avoid the hazards of general anaesthesia in these patients.

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It has never been clear to me why some anaesthetists are so afraid to give suxamethonium to a patient who is known to have a low level of cholinesterase activity and who is required to undergo a surgical procedure which is likely to last longer than a few minutes. Among the specific skills of anaesthetists is the ability safely to maintain the ventilation of a paralysed patient, and suxamethonium has no toxic properties other than a well-circumscribed potential for causing bradycardia.

Based upon a continuing collaboration with Dr Mary Whittaker, my strong suspicion is that the true incidence of a low level of cholinesterase activity due to a genotype variant is closer to 1:300 than to the oft-quoted ratio of 1:2000. Our observations derive from studies of patients given general anaesthesia in this hospital, in which the technique almost invariably includes the intravenous infusion of suxamethonium from beginning to end of the operation. Despite literally thousands of such cases, we have encountered only three or four in which recovery from the action of suxamethonium was delayed for approximately 30 minutes and there has been one in which there was a 2-hour delay. In the remainder, a delay of 15–20 minutes prompted an assay of cholinesterase activity, which almost invariably provided a positive result.

A quarter-century ago, whilst holding an appointment in Aberdeen, I spent a 6-month period in which I gave all the anaesthetics administered in the Maternity Hospital, including over 200 for Caesarean section (operating time 45–60 minutes). With middle-aged enthusiasm I gave these mothers, on average, 600–800 mg suxamethonium by infusion, in addition to the 100 mg induction dose. Not infrequently the total dose exceeded one gram. In only three cases did the mother fail to lift her head more than 2 inches from the pillow within 10–15 minutes of my stopping the infusion. In two of these, the mother's level of cholinesterase activity was subsequently found to be abnormally low and in the third the result of the test was equivocal. I have since remained unconvinced that the concept of dual block has any clinical relevance.

The decision made by Dr Morrison and his colleagues (*Anaesthesia* 1986; **41:** 323–4) was, in my opinion, wrong. Even had the mother's level of cholinesterase activity been close to zero she would have required supportive ventilation for no longer than an hour or two postoperatively—so what? If they were worried about the prospect of a difficult or failed intubation in the context of delayed recovery from the relaxant, then surely atracurium was an equally inappropriate choice, in that it is hardly likely that its action would be reversed in less than 10–15 minutes after administration. The alternative, and a second-best, was induction and maintenance using an inhalational technique, with the mother in the full left lateral position, as in an advocated component of the failed intubation drill. The third best choice, if consideration is given only to general anaesthesia, would have been an awake intubation.

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Test dose for spinals

Dr Mallaiah (*Anaesthesia* 1986; **41:** 334) states that, based on his experience of 100 patients using 0.5% plain isobaric bupivacaine, he does not consider that 1.5 ml of 0.5% bupivacaine is a suitable test dose. He does not state the type of patients or the nature of the operations. In our previous correspondence we were writing strictly about obstetric patients and therefore cannot compare our findings with Dr Mallaiah's small, undefined series.

However, in a series of over 500 patients for Caesarean section, I can merely reiterate that 1.6 ml 0.5% bupivacaine injected through a 26-G needle with the patient being returned to the supine position with lateral tilt after injection, consistently produced a block to T_{10} within 3 minutes and a high thoracic block within

5–10 minutes. Our experience using this technique for other types of surgery tends to suggest that size of needle and speed of injection do make a difference to speed of onset and level of block. However, in our quoted series, the above were standardised.

With reference to the practice of using 2 ml 5% lignocaine in obstetrics, it has been our experience that this dose produces a high incidence of unacceptably high motor block causing respiratory difficulty and is therefore not to be recommended.

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Retinal haemorrhage following laparoscopy

Minor visual disturbances of short duration are relatively common after anaesthesia. More serious ophthalmic complications are rare. This is a report of an unusual complication after laparoscopy.

The patient was a 30-year-old, 61-kg woman who, 3 years previously, had undergone an uneventful general anaesthetic for dental extraction. She smoked twenty cigarettes per day and her only medication was an oral contraceptive. Medical history, clinical and laboratory examination were all unremarkable.

Premedication was with papaveretum 15 mg and hyoscine 0.3 mg intramuscularly. One hour later anaesthesia was induced with intravenous thiopentone 250 mg, followed by atracurium 25 mg and pentazocine 30 mg. The lungs were ventilated with 67% nitrous oxide in oxygen by facemask for 2 minutes and the trachea was intubated. Ventilation of the lungs was controlled using the Bain system and a Penlon Nuffield ventilator with a tidal volume of 600 ml and a fresh gas flow of 100 ml/kg/minute at a frequency of 10/minute. No supplementary inhalational agents were used.

Laparoscopy was performed without complication by insufflation of intraperitoneal carbon dioxide in the Trendelenberg position and, at the end of surgery, residual neuromuscular blockade was reversed with neostigmine 2.5 mg and atropine 1.2 mg intravenously. The total duration of anaesthesia was approximately 20 minutes and the recovery period was uneventful; the patient was discharged home the next day without any complaint.

Six days later she reported to her general practitioner and complained of limited vision in her left eye; she stated that she had awoken after operation with a grey shadow across both eyes, although the right eye had cleared within an hour. She was referred to the ophthalmic department, where fundoscopic examination revealed bilateral papilloedema and retinal haemorrhages, particularly in the left eye, where they involved the macula. Vision was 6/6 in the right eye (OD) and 6/60 in the left (OS). Four weeks later, the haemorrhages had been absorbed but there was a residual scar-like spot on the macula. Vision was 6/6 OD and 6/60 OS, which improved to 6/18 after a further 4 weeks. Four months after her laparoscopy vision was 6/6 in both eyes.

There are several possible reasons why retinal haemorrhage could occur during laparoscopy. The first is the use of steep Trendelenberg tilt; retinal haemorrhages have been described in 20% of patients undergoing air encephalography in the head-down position,[1] but not in patients maintained supine.[2] The dependent position causes a rise in cerebral and retinal venous pressure and other factors, such as hypoxia, hypercarbia and the use of volatile anaesthetic agents, compound this by retinal venous dilatation. Coughing, vomiting, obstruction to venous return of the head and neck, and tracheal intubation also raise intracranial and retinal vencus pressure. It is recognised that the insufflation of carbon dioxide or nitrous oxide into the peritoneal cavity, to a pressure of 20 mmHg, causes a rise in right atrial pressure[3] and this also tends to increase intracranial pressure.

Retinal venous haemorrhage can occur in normal healthy individuals[4] and has been attributed to a Valsalva manoeuvre during episodes of protracted vomiting or activities such as blowing up balloons or inflatable toys.[5] There were no episodes of bucking or straining in this patient, although this does not exclude a rise in intracranial pressure at tracheal intubation. There were no prolonged episodes of postoperative vomiting. Ventilation was controlled using the Bain system and a fresh gas flow known to result in moderate hypocarbia, so it is possible that, following the intraperitoneal insufflation of 2–3 litres of carbon dioxide, there was significant hypercarbia. It is well recognised that hypercarbia may occur during laparoscopy, despite moderate hyperventilation and, furthermore, since peritoneal absorption of carbon dioxide is a relatively slow process, peak arterial $P\text{CO}_2$ levels may not be reached until up to 15 minutes after insufflation, perhaps at a time when the patient is in the recovery ward.[6,7] Pneumoperitoneum and the Trendelenberg position, by causing diaphragmatic elevation and altered ventilation–perfusion relationships of the lower lobes, may further contribute to hypercarbia, although this is less likely during controlled ventilation.[7]

There are therefore several factors present during laparoscopy which tend to increase retinal venous pressure and, if a further pressure surge, such as an involuntary Valsalva manoeuvre or a bout of coughing or vomiting, is superimposed on this raised pressure, rupture of the retinal microcirculation becomes very likely.[8]

A defect in vision is noticed by the patient only when the macula is involved. Furthermore, many patients may not volunteer information, accepting that some degree of visual impairment is not uncommon following anaesthesia.

This case report, and one other almost identical report,[8] might lead one to suspect that cases of visual impairment following laparoscopy are more common than they appear.

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Computerised tomography guided lumbar sympathectomy

The paper by Dr Redman and colleagues (*Anaesthesia* 1986; **41:** 39–41) was very interesting and I would like to comment briefly on the technique and its usefulness in routine patient care in District General Hospitals.

The complications listed can be minimised by preoperative assessment: clinical examination, simple investigations like abdominal X ray, ultrasound and the use of 20-G 12 cm needles except in tall and obese patients.[1,2] A standard technique for paraveretebral lumbar sympathetic nerve block is used.[1,3,4]

It is difficult to position patients with painful ischaemic legs, especially in the prone position, and they are more comfortable during the procedure if they rest on the relatively normal side.[1] There is no reason for patients to be nursed for 4 hours in the prone position.

This block is done on my routine operating list. Most of the patients are elderly.[5] They are given a light, early-morning breakfast and come to the operating room without premedication.[1] An intravenous infusion is established with Dextran 70 and diazepam is given in small doses for sedation. The position of the patient is maintained for 20 minutes on the operating table after the neurolytic injection. They are then transferred to the ward to be nursed supine for 12 hours with intermittent trial of sitting to avoid hypotension. Once the arterial pressure is stable, the infusion is removed and the patient leaves hospital the next day.

Computerised tomography guided chemical lumbar sympathectomy is a very useful technique, but it is not feasible in most District General Hospitals. One can still perform this very effective and simple procedure by proper selection of patients and the use of a standard technique with either image intensification or X ray facilities available in all hospitals. Those patients with associated problems like aortic aneurysm, renal cyst and gross spinal deformity should be sent to the special centres where appropriate measures can be taken.

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A reply

Thank you for the opportunity to reply to Dr Singh's letter. The purpose of our article was to refine the technique of chemical lumbar sympathectomy and to describe a different method which is useful in complicated cases. Furthermore, computerised tomography scanning facilities will undoubtedly become more widely available in the future.

We agree that it is sometimes difficult to place these patients in the prone position, but all the patients in our

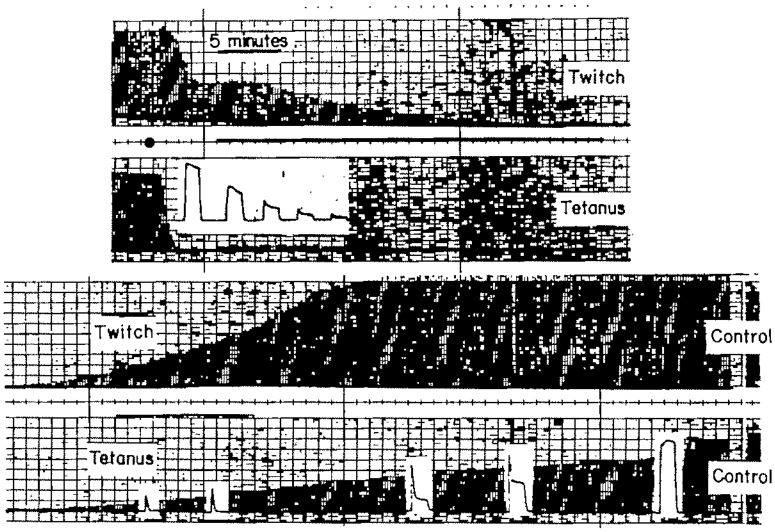

Fig. 7. Illustrates the use of a continuous infusion of vecuronium to maintain neuromuscular block and the pattern of recovery of the tetanic and single twitch responses after the infusion was discontinued. Patient: sex, male; age, 23 years; weight, 75 kg. Anaesthesia: induction, thiopentone 500 mg intravenously; maintenance, N_2O 6 litres; O_2 4 litres; halothane 0.5%. Vecuronium: bolus 0.02 mg/kg; infusion 0.002 mg/kg/minute.

It is tempting, in the autumn of a career largely devoted to clinical research, to pontificate on how such work should be continued and expanded. I will resist that temptation and merely reflect that John Hunter's advice to Edward Jenner not to think but to try the experiment has stood the test of time. In paying tribute to John Hunter, I recognise that in the state of knowledge of his time my title, *In Pursuit of Relaxation*, would have had little interest for him, but I like to think that he would have been quick to recognise its surgical significance had the times been right. Equally, I accept that in the context of his own lifestyle, despite his history of angina, relaxation would have had no place. Notwithstanding every effort made by his friends and advisers to protect him, John Hunter exercised his own right to ignore advice that he found unpalatable, although he had to admit that 'my life is in the hands of any fool who cares to upset me' and so it was. Controversial to the end, he died in a rage provoked by some of his colleagues at a medical committee meeting at St George's Hospital on 16 October 1793. There are less pleasant ways to die.

Acknowledgments

In the period under review I have been indebted to a very large number of colleagues, medical, nursing and technical, for their cooperation and support. Many have been acknowledged in the list of references but a few who have not been so recognised should be mentioned. Over the past 10 years Miss V.A. Bishop, SRN, MPhil, has provided invaluable nursing support and Professor J.P. Blandy has always been prepared to adjust his operating list to accommodate the research programme. To both I express my very deep appreciation. To all others who have given me assistance in so many ways I am equally grateful.

Finally, I acknowledge the courtesy of the Editors of the *Journal of Applied Physiology*, the *Journal of Clinical Pharmacology*, and the *British Journal of Anaesthesia* for permission to reproduce figures published in their journals.

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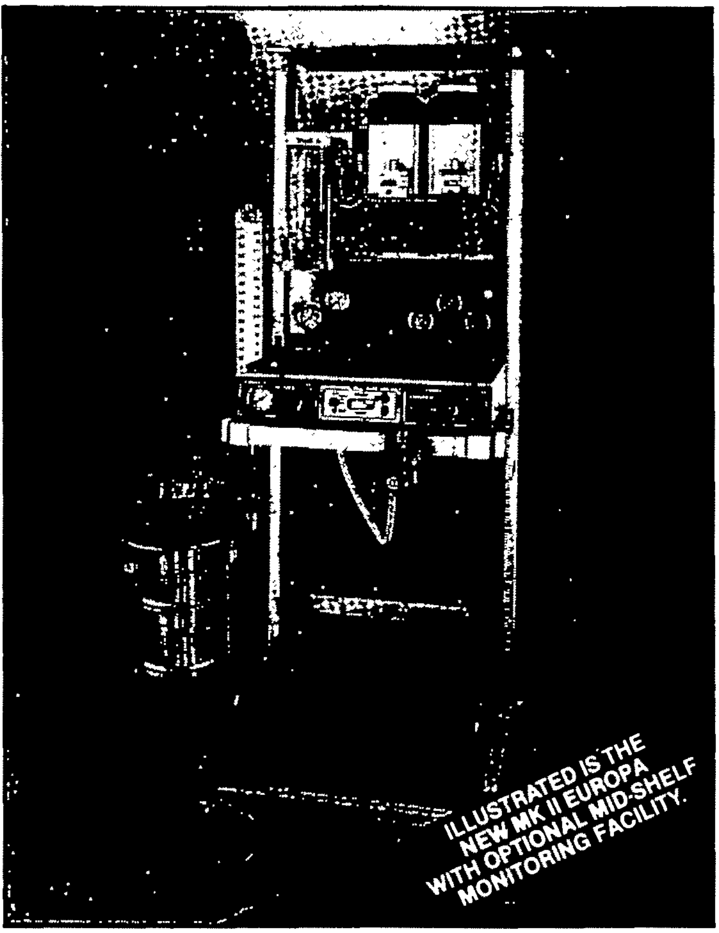

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Clinical Controversies in Neuroanesthesia and Neurosurgery

M. JANE MATJASKO, M.D., and JORDAN KATZ, M.D.

This unique new multi-authored text presents clinical controversies in neuroanesthesia and neurosurgery, and suggests alternatives for providing optimal patient care.

The authors, experienced clinicians in their fields, are encouraged to logically and completely delineate the problem, review the current literature, and suggest possible treatment options for five main areas of controversy. A chapter on ischemic cerebrovascular disease presents the pathogenesis, diagnosis, and treatment of the disease and analyzes the operative anesthetic, and postoperative management principles related to carotid endarterectomy, extra-cranial and intra-cranial bypass. The challenge presented by acute spinal cord injury is addressed beginning with initial management assessment of respiratory and cardiac function, and long term care. The controversies regarding the physiopathology monitoring and anesthetic of severe head injury are discussed in detail. Supratentorial and infratentorial tumors including controversies related to the seated position and various aspects of the perioperative care of aneurysms are presented in depth.

Clinical Controversies in Neuroanesthesia and Neurosurgery offers the most informative and authoritative view of this field to date. It will be a valuable reference for anesthesiologists, neurosurgeons, neurologists, and other professionals involved in the care of neurologically compromised patients.

CONTENTS: Foreword. Preface. Acknowledgements. Contributors. *Betty L. Grundy and Roberto Heros,* Ischemic Cerebrovascular Disease. *Colin F. Mackenzie and Thomas B. Ducker,* Cervical Spinal Cord Injury. *Robert Bedford and Peter Colley,* Intracranial Tumors. *Jane Matjasko and Lawrence Pitts,* Controversies in Severe Head Injury Management. *Adrian W. Gelb and Philippa Newfield,* Intracranial Aneurysms. Index.

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series were able to cope with this situation and settled well with incremental doses of intravenous diazepam and fentanyl. Some patents cannot pass easily into the scanner if they are in the lateral position. It is also convenient to perform bilateral blockade in the prone position.

Dr Singh's technique using image intensification is standard practice and we are not advocating that it be abandoned. We do not, however, see any need for the use of a dextran 70 infusion (with its attendant dangers) and hypotension has not been found to be a problem in two large series of chemical lumbar sympathectomies.[1,2] Analgesics, although not essential, are anxiolytic and are useful in alleviating pain that may arise during the block. We also do not consider it to be necessary to do a pre-operative abdominal X ray and ultrasound examination before the procedure.

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Anxiety levels in junior anaesthetists

We read with interest the paper from the Leicester department (*Anaesthesia* 1986; **41:** 258–62). It would seem foolhardy, however, to draw any conclusions from a study of only four individuals. This is further borne out by the fact that three out of the four individuals studied had a trait anxiety level more than one standard deviation below the expected norm.

These results, and the apparent lack of responsiveness in terms of measured state anxiety in various situations, bring into question the accuracy of the measures. The reported increase after a verbal warning is an interesting anomaly. Self reporting of perceived anxiety levels may have been a useful adjunct. Publication of actual recorded heart rate and arterial pressure may also have been useful, rather than the statement that no significant changes occurred. The individuals studied may have been subject to less anxiety than normal adult males, an issue which in itself might be addressed, or it may be that they were stressed at all times and that the measures used and the person administering the assessments were not sensitive enough. Certainly, the stressful existence of junior anaesthetists warrants further study.

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A reply

We are pleased to read that Drs Linter and Linter found our study sufficiently interesting to warrant communicating with the Editor. However, we cannot accept that measurements of heart rate and arterial pressure warranted reporting since these are notoriously inaccurate in the assessment of anxiety. The tests which were utilised in our study are well recognised and acceptable as sensitive indices of trait and situational anxiety and the purpose of our study was to undertake a pilot investigation within our own Department of only the transitional period in training after the first 3 months' exposure to anaesthesia. It would be quite ridiculous to imply, as we certainly have not, that the practice of anaesthesia by junior anaesthetists is not associated with stress. However, we would suggest that for uncomplicated, routine, minor anaesthesia, it is not stressful to go solo after a 3-month period of training. It is highly likely that the presence of anaesthetic complications would provoke severe stress, but that was not the purpose of our investigation.

We also proposed in our paper that further studies should be undertaken of stress during anaesthetic training and we look forward to seeing the contributions of Drs Linter and Linter in this area.

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Hazards of heated water humidifiers

The letter by Dr Smith and Dr Allen (*Anaesthesia* 1985; **41:** 215–6) about the dangers of heated water bath humidifiers with continuous flow through ventilators is useful in serving to remind readers of this potentially very serious hazard.

This is not a new problem. Despite the presence of thermostats and other safety devices, it is well recognised that scalds may occur if the rate of delivery of humidified gas suddenly increases, so that there is less time for cooling in the delivery tube.[1] This may well occur in ventilator systems in the situations described by Drs Smith and Allen, when an intermittent flow is suddenly converted to a continuous high flow during patient disconnexion.

Some 10–15 years ago, we had experiences of scalds to patients from continuous flow from Bird Ventilators through Cascade humidifiers during disconnexion for tracheal suction. Since changing to the Fisher and Paykel Humidifier,[2] in 1973 and subsequently to the Grant Humidifier,[3] we have not experienced this problem. Both these humidifiers limit the temperature of the water in the waterbath to safe levels, whilst still reliably delivering 100% saturated gas at body temperature at the patient end of the system, with no rain-out in the delivery limb. Such performance is necessary, particularly when treating newborns and small infants, to prevent blockage of small tracheal tubes with inspirated secretions. The use of these humidifiers has made the occurrence of such complications almost unknown in our neonatal unit in the last 13 years, despite the fact that we do not routinely change tracheal tubes, many of which remain in place continuously for weeks at a time.

More recently we have been assessing the use of
and moisture exchangers (HMEs) in paediatric a
thesia and believe them to be satisfactory for r
routine anaesthetic uses. However, we do not be
that they will replace proper humidification in
intensive care of small infants and children requ
long term artificial airway support.

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Medical gas probes

We would like to bring attention to a potential hazard with the noninterchangeable quick coupler system used for the delivery of medical gases. The male component of the system comprises a standard, stainless steel probe with retaining groove. The noninterchangeability of the probe is dependent on an indexing collar with specific internal and external diameters according to the gas carried. The British Standards Institution requires that the indexing collar be irremovable from the probe! This can be achieved with a steel collar by welding. Cheaper alloy collars are unsuitable for this treatment and are attached to the probe by a form of friction fitting.

Figure 1 is a photograph of a medical air probe discovered during routine maintenance. The alloy collar had worked loose with constant use and could easily be detached from the probe by hand. Should the indexing collar actually fall off, the probe could then be inserted into any of the standard gas or suction terminal units. The potential consequences of such a misconnexion need no further elucidation.

Several probes with dangerously loose friction fit alloy collars have now been found in two separate hospitals in this study. The Department of Health and Social Security has been informed of the hazard. In view of our findings we strongly discourage the use of the friction fit type of indexing collars and recommend careful examination of all such probes currently in use.

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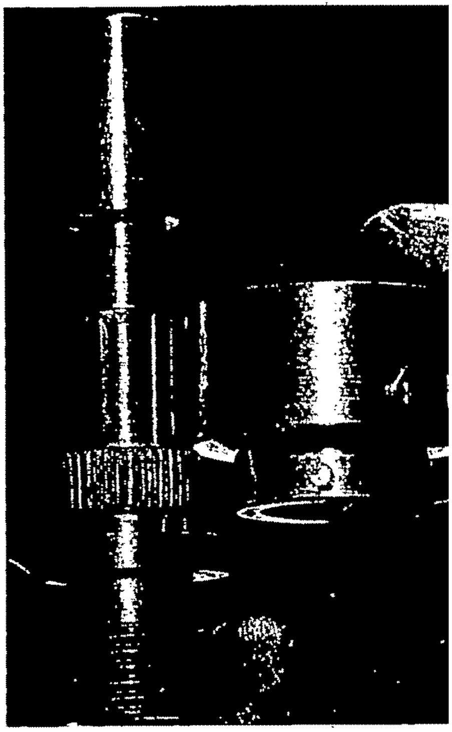

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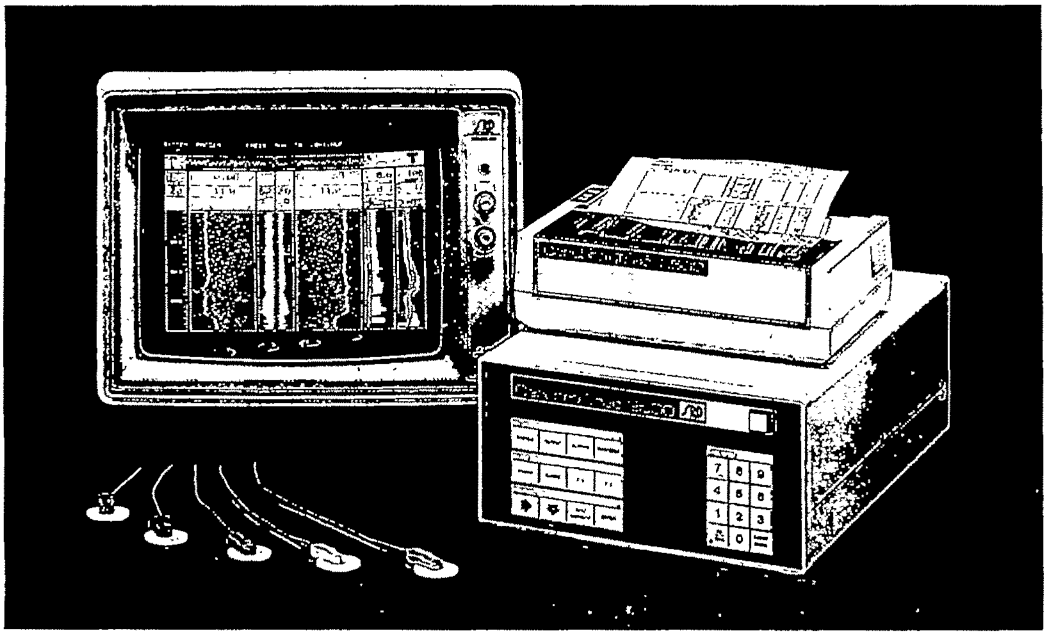

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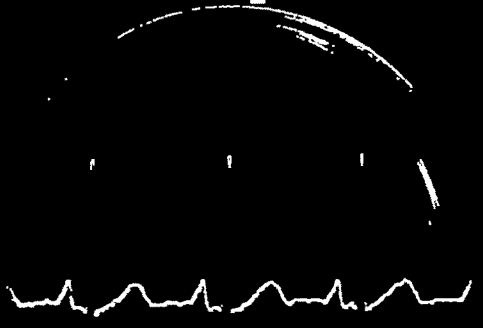

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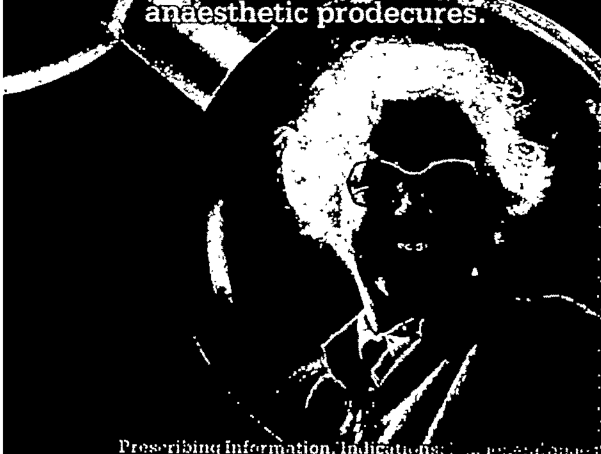

AErrane™ (isoflurane) is not approved for use in obstetrics.

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Prescribing Information. Indications: [illegible] **Dose:** [illegible] **Contraindications:** Known sensitivity to AErrane™ [illegible] **Side Effects:** Hypotension, respiratory depression, arrhythmias, elevated white blood count, shivering, nausea, vomiting and ileus [illegible] **Product Licence Number:** [illegible]

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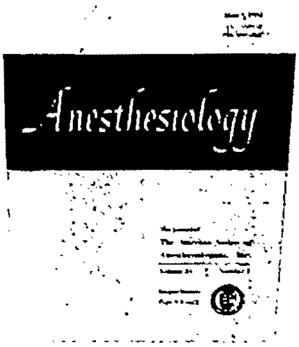

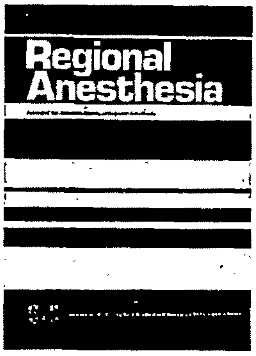

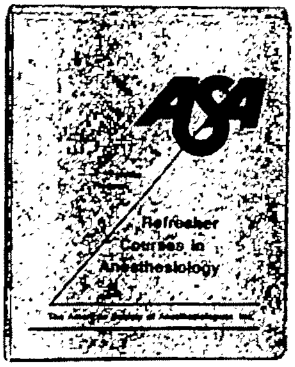

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Successful treatment of inadvertent intra-arterial injection of antibiotics

Inadvertent administration of drugs into a cannulated radial artery remains a hazard which may have disastrous consequences. Accidental intra-arterial injection of 500 mg of flucloxacillin which resulted in gangrene that necessitated partial digital amputation and skin grafting of the arm 8 weeks later has been reported.[1] Immediate treatment consisted of intra-arterial administration of lignocaine, heparin and intravenous dextran 70. Stellate ganglion blockade was performed 6 hours after the incident.

We wish to report a similar incident in a 37-year-old man who had undergone a lumbar decompression following a crush fracture sustained in a road traffic accident. Flucloxacillin 1 g in 10 ml water and sulphadimidine 1 g in 10 ml water were inadvertently administered intra-arterially in the postoperative ward. The patient immediately complained of pain in the forearm and hand. The resident anaesthetist was informed and treatment was commenced within minutes. This consisted of intra-arterial administration of 20 ml of heparinised saline, 15 ml of procaine 0.5% followed by a stellate ganglion blockade. A hyperaemic area measuring 8 cm × 4 cm was noted on the radial aspect of his distal forearm. The hyperaemic area regressed within 12 hours, leaving a small dark red area. Long term anticoagulation was considered inappropriate after the type of surgery undertaken. Twenty-four hours later the patient complained of numbness of the third finger and a decreased hand grip and finger abduction were noted. The radial pulse was always present. Over the next 2 days, repeated stellate ganglion blocks were performed followed by a continuous brachial plexus blockade for the subsequent 3 days. This was administered by inserting a 20-G cannula into the patient's brachial plexus sheath via an axillary approach. Bupivacaine 0.375% was infused via a syringe pump to provide sympathetic blockade and pain relief. Eight ml/hour was found to be the optimal infusion rate.

Two weeks following the injury, the mottled area sloughed off and the necrotic zone healed spontaneously within 8 weeks. At the time of writing there remains a slight diminution of sensation of the thumb, index and middle fingers. There is no residual motor loss in the hand. The patient is able to use a wheelchair.

The result of this treatment is dramatic in comparison with the previous report. Sulphadimidine is unlikely to have a dilutional effect as it forms a crystalline precipitate at a pH of less than 10 and may have a similar effect to thiopentone.[2] The mechanism by which drugs damage arteries appears to be multifactorial and has not been fully elucidated, but arterial spasm, endothelial damage, intra-arterial thrombosis and endoarteritis subsequently develop.[3,4]

Prompt management and persistent sympathetic blockade to alleviate arterial spasm and promote blood flow may be responsible for averting a potential disaster.

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Diluting suxamethonium

We were interested in the letter from Dr Nickalls, (*Anaesthesia* 1985; **40:** 225), about the potential problem following dilution of suxamethonium before use.

We are fortunate to spend time each year giving anaesthesia for a plastic surgery group working in various South and Central American countries. A perennial problem, as Dr Nickalls point out, is the loss of potency of suxamethonium ampoules, especially at temperatures that may vary widely. We seem to have overcome this problem by using the powder 1000 mg diluted in 200 ml saline. This solution remains active for several days and, so far, we have not encountered any problems due to loss of potency of the drug when mixed in this manner.

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Intravenous regional anaesthesia with ketamine

The article (*Anaesthesia*, 1985; **40:** 899–900) by J.F. Amiot and colleagues, prompts me to ask one question: could physostigmine be used as an antidote for the unconsciousness caused by betamine? Balmer and Whyte[1] have shown experimentally that physostigmine reverses the psychomimetic effects of ketamine and Toros-Matos *et al.*[2] discovered that physostigmine shortens the recovery time of ketamine. The cardiac side effects of the probably necessary higher doses of physostigmine may limit this reversal.

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A reply

Ketamine interacts with brain cholinergic receptors of the muscarinic type.[1] The reduction of the acetylcholine turnover rates in the caudate nucleus and hippocampus partly explains the central nervous effects of ketamine.[2] However, several investigators have tried to antagonise the sedative and anaesthetic actions of ketamine with physostigmine, which acts centrally as an active cholinesterase. We have not used physostigmine as an antidote to the ketamine-induced unconsciousness following the release of tourniquet, because the early results were contradictory.

Toro Mayos *et al.*[3] have shown that physostigmine shortens the recovery time of ketamine. Others have found that physostigmine does not reverse the central nervous system effects produced with anaesthetic doses of ketamine.[4] Figallo and Wingard[5] demonstrated that physostigmine prolonged ketamine-induced sle time in rats. That was foreseeable, since the n chemical mechanisms underlying the anaest analgesic and psychomimetic properties of ketami multiple.[6]

Our aim was the complete suppression of the l consciousness after the release of tourniquet; that i the study of Stella *et al.*[7] had seemed interesting.

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J.H. PA
J.F. A

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A new integrated suction laryngoscope

The Macintosh laryngoscope blade was first described in 1943.[1] Several derivatives of the Macintosh design have since been developed for the management of specific clinical problems, although most are unsuitable for routine use. This is a description of a modified Macintosh laryngoscope blade which has several useful clinical applications, but may also be used for routine laryngoscopy.

The modification consists of the incorporation of a stainless steel tube onto the lingual surface of a standard Macintosh laryngoscope blade (Fig. 1). The tube, which opens into a slot at the tip of the blade (Fig. 2), is attached to a vacuum source by plastic tubing either directly or via a Y-connector to facilitate control of suction. The instrument may be regarded as a suction laryngoscope or a laryngoscopic sucker, depending upon its principal application. The suction conduit does not interfere with or obstruct laryngoscopy. N does it, of itself, contribute to trauma to teeth or t of the mouth. Disinfection and cleaning are no difficult than for an unmodified blade, since the l is accessible to small flexible brushes such as thos for cleaning fibreoptic endoscopes.

Clinical experience with the new laryngoscop shown it to be useful in routine anaesthesia for all of surgery, but particularly in dental, ENT an premedicated cases. The ability to remove bloo secretions easily and simultaneously with laryngos thus leaving one hand free for removal of pack other manoeuvres, is a great advantage. An inci benefit is economy in the use of pharyngeal suck

The desirability of simultaneous suction laryngoscopy during induction of anaesthes patients at risk from regurgitation of stomach con

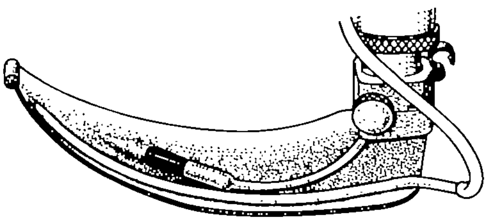

Fig. 1. Drawing of the new blade. Plastic tubing attached to the end of the suction conduit leads to a vacuum source via a Y-connector taped to the laryngoscope handle.

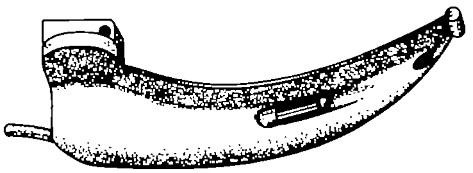

Fig. 2. The new blade showing the orifice of the suction conduit at the tip.

and thus pulmonary aspiration, has previously been stressed.[2] The suitability of this design for obstetric and emergency anaesthesia is clear. Substitution of the vacuum for fresh gas flow from an anaesthetic machine allows the delivery of oxygen or an anaesthetic gas mixture to the patient during laryngoscopy, thus providing a potentially useful aid during prolonged or difficult intubation.

Mr P. Hodt of the Medical Physics Department of St George's Hospital has helped me in the production of this prototype.

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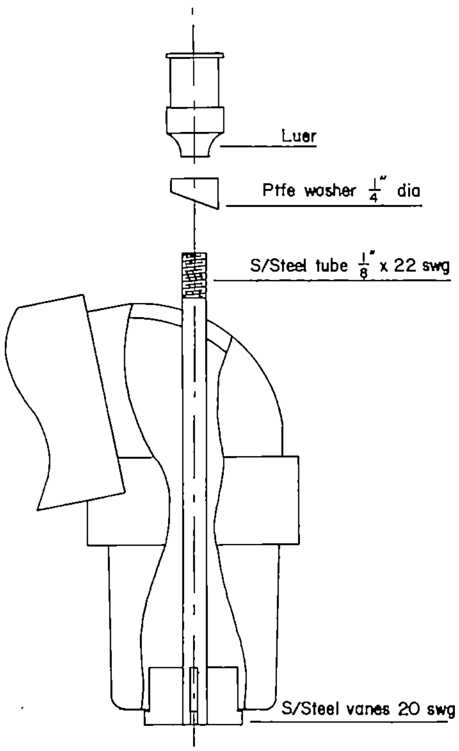
Gas sampling from a facemask for capnography

Capnography has been under utilised in clinical anaesthetic practice until recently; however, it may provide a measure of ventilation, pulmonary perfusion and carbon dioxide production.[1,2]

The site of sampling for capnography is important;[3] in the intubated patient, sampling should be performed close to the carina if tidal volumes are small relative to dead space, or from the top of the tracheal tube if tidal volumes are large.[4,5] Patients without a tracheal tube may have samples taken from the nostril.[3]

In practical anaesthesia, a modified angle piece, as illustrated (Fig. 1) provides a convenient Luer connexion from which sampling of the undermask space may be undertaken. The hub of a spinal needle is drilled out and tapped so as to screw onto a threaded stainless steel tube which is held distally by three flanges. The hub seats on a teflon washer which is sealed with silicon rubber and the screw is coated with locking fluid before being tightened to produce a gas-tight seal.



Luer
Ptfe washer $\frac{1}{4}''$ dia
S/Steel tube $\frac{1}{8}''$ x 22 swg
S/Steel vanes 20 swg

Acknowledgment

We should like to thank the Department of Medical Physics, Raigmore Hospital, Inverness, for their help in constructing this device.

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Bronchoscopic intubation in children

We read with interest the letter about the use of a biopsy brush wire as a bronchoscopic guide (*Anaesthesia* 1986; **41:** 444). Fibreoptic bronchoscopy in experienced hands has much to offer as an aid to intubation in difficult circumstances; one is, however, limited by the size of tracheal tube which one can fit over the bronchoscope. For example, when using the Olympus BF Type IT10 intubating bronchoscope, which has an O.D. of 6.0 mm, the smallest tube which may be introduced over this is 7.0 mm I.D. The paediatric intubating bronchoscope has an O.D. 3.6 mm, so the smallest tube which may be used is 4.5 mm. Therefore one cannot use it in neonates.

There are two points in the original letter which we feel deserve comment. Firstly, a brush biopsy wire could cause significant trauma to tracheal mucosa, all the more so in a small patient. We propose that the suction channel of the adult bronchoscope may be used to pass a monofilament nylon bougie (2 mm diameter) which should be about 30 cm longer than the bronchoscope. The bougie is introduced into the trachea once the larynx is seen through the bronchoscope. The latter is then removed, keeping the guide stilette securely in place. Any tracheal tube may then be passed over it.

Secondly, it is inappropriate to use sedation and local analgesia in children, but the authors do not mention how the child is to tolerate bronchoscopic intubation. One technique is as follows. The baby is kept asleep breathing oxygen and a volatile agent using a Rendell Baker-Soucek mask. The bronchoscope is passed through a sealing swivel connector (Portex, Double Swivel Connector Ref. No 100/255/000), which allows the baby to breathe spontaneously throughout the procedure.

A particular point to notice is that this technique allows the use of an adult bronchoscope for intubation with the complete range of tracheal tubes. The narrower bronchoscopes of course allow small sized tubes to be passed over them, but they do not have a suction channel that can be used as described, thus restricting their application. The versatility of this technique is depicted in Fig. 1.

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Fig. 1. Range of size of tracheal tube compatible with various bronchoscopes

Size of tracheal tube to be used (mm)	2.5	3	4	5	6	7	8	9	10
Standard fibreoptic bronchoscope						---	---	---	---
Intubating laryngoscope					---	---	---	---	---
Paediatric bronchoscope				---	---	---	---	---	---
Guide stilette	---	---	---	---	---	---	---	---	---

Difficult intubation in obstetrics

Dr Cormack's statistical expertise is well known and I do not seek to challenge his arithmetic (*Anaesthesia* 1986; **41:** 332–3), but I hope he does not expect me to thank him for calculations that show I must work until I am 90 years old before my point becomes valid in statistical terms!

While we are waiting, it might be worth examining the issues. Dr Cormack proposes tackling difficult intubation by blind intubation over a gum-elastic bougie and teaches this by simulating difficulties on low-risk patients.[1] He cannot provide evidence that this is beneficial, but it is an approach that appeals to common sense and deserves to be widely adopted. No matter what preparations are made, some intubations will fail. Judging from Dr Cormack's writings, he also believes in a drill to cope with this event.[1] Differences of philosophy provide the basis for debate and our difference, perhaps, lies in our readiness to employ a failed intubation drill. However, as any statistician will know, solutions to problems are found not through the expression of opinion, but by the collection of facts and figures.

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Editor's note: this correspondence is now closed.

Ugandans, Uganda needs you

There are a number of Ugandan anaesthetists in Europe and elsewhere. Uganda needs them here at home, where an era of peace and security, and economic recovery too, we hope, have begun. It is not appropriate for a foreigner to invite these people to return to their own country, but perhaps one can challenge them. It will not be an easy task; conditions of work will lack much that they now take for granted. Their skill and ingenuity will be put to the test and they may often be frustrated and even discouraged. However, the first moves have been made to re-establish a proper department of anaesthesia at the Mulago Hospital in Kampala and the presence of Ugandans, either with their FFARCS diploma or its equivalent, would do much to guarantee the success of this venture.

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Anaesthesia, 1986, Volume 41, pages 974–977

Book reviews

Anaesthesia Review 3 974
Edited by L. Kaufman
Hypothermia and Cold Stress 974
E.H. Lloyd
Clinics in Anaesthesiology. Current Topics in Intensive Care 975
Edited by E. Dobb
Resuscitation. Care of the Critically Ill, 2nd edition 975
D.K. Brooks
Perinatal Anesthesia (Contemporary Issues in Fetal and Neonatal Medicine) 976
Edited by J.W. Scanlon

Anaesthesia Review 3
Edited by L. Kaufman. Pp. 216. Churchill Livingstone, 1985. £14.00.

The third in this series of books continues the tradition set by its predecessors of producing a collection of recent reviews concerning various aspects of medicine pertaining to anaesthesia. Inevitably, there is variation in both style and quality of contribution.

There are 17 chapters, but 15 topics. Blood transfusion and blood products are described in two separate chapters (it is not clear why, since the same authors wrote both), in which a wealth of information is provided about the latest technological advances in component therapy. However, haematologists never seem prepared to commit themselves as to the possible adverse effects of transfusing large amounts of protein-reduced blood into the acutely bleeding patient and the authors of these chapters are no exceptions. There are two chapters dealing with obstetric anaesthesia. The first of these is an excellent update for those who do not deal regularly with obstetric practice. The purpose of the second (written by the editor) is unclear; although some new topics are introduced, there is considerable overlap between the two.

The need for anaesthetists to keep abreast of advances in medicine is met by two chapters dealing with myopathies and myasthenia gravis and a miscellany of recent developments. The assessment of cardiac risk in patients undergoing noncardiac surgery is summarised in a succinct and very readable contribution. The interactions between anaesthesia and the liver and the problems associated with anaesthesia for hepatic surgery are described, although a description of the general management of patients undergoing liver transplant would have been desirable, as this procedure is becoming rather less uncommon than was the case and many anaesthetists may become involved either in the operating theatre or intensive care unit within the next few years.

Two separate chapters discuss opioid receptors and endorphins in a welcome attempt to decipher these complex subjects into an intelligible form. The new muscle relaxants, including those not yet available in Western Europe, are described. All examination candidates should read the excellent article appraising inhalational anaesthetic agents.

The assessment of the brain during anaesthesia is reviewed, and there is a very clear account of the alterations in gas exchange during anaesthesia. The management of patients with burn and smoke inhalation injuries is discussed and there is a chapter outlining current thinking on cardiopulmonary resuscitation. The book concludes with an update on topics presented in the previous volumes.

Once again, Dr Kaufman has produced a book with something for every anaesthetist. Apart from avoidable repetition, there is little to criticise. It is almost impossible for most anaesthetists to keep pace with world literature in all fields related to anaesthesia, and collections of review articles serve an important function in summarising new information and relating it to established work. Inevitably, both examiners and examination candidates will want to read this book. However, its readership should not be confined to those destined for Lincoln's Inn Fields.

A.L. Aitkenhead

Hypothermia and Cold Stress

E.H. Lloyd. Pp. 400. Croom Helm Ltd, 1986. £27.95.

This is a timely publication by an author who has spent many years studying this subject and various aspects of rewarming. His stated intention is to provide a reference book for those 'front line' staff who have to manage the hypothermic patient. The book is divided into four parts: the first two parts occupy almost half of the text and deal largely with the pathophysiological effects of exposure to cold; parts three and four are concerned with treatment in general and then in specific situations.

The first thing that struck me about this book was that it is incredibly well researched. The bibliography extends for almost 54 pages after the text. Initially the references seemed to break up the prose at times, but later I used the list frequently to earmark further reading. The index, tables and illustrations are also quite adequate.

The first section deals mainly with definitions, thermoregulation and mechanisms whereby heat can be lost to a significant extent. Towards the end there are some pertinent observations concerning the potential pitfalls in rescue and transport of the hypothermic victim to hospital. Part two is largely concerned with the pathophysiology of cold stress on skin, limbs and cardiorespiratory system and on cerebral performance. This is a very wide-ranging section and extends from an excellent little piece on Trench Foot to some thoughts about infant cot death syndrome.

The second half of the text is, in the main, devoted to clinical management. There is an initial review of the advantages and problems of spontaneous rewarming, followed by similar chapters on each of the various methods of active rewarming processes, including a very comprehensive one on airway warming. The controversial problem of resuscitation in severe hypothermia is still a difficult area; the various views are carefully and fairly considered, although the conclusions indicate that more work remains to be done in this field.

The final section of the book considers the effects of cold in particular areas and includes hypothermia in the elderly and immersion problems. There is also a short chapter on hypothermia in relation to anaesthesia and various aspects of potential cold damage during outdoor activities.

What criticisms I have of this book are small; perhaps the later chapters of physiology could be pruned to allow a little more consideration of the commoner clinical situations, such as treatment of hypothermia in the elderly and immersion problems. Overall, however, I think this book has achieved its aims and should be readily available to those working in casualty and intensive care units in this and many other countries.

A.D. SIMCOCK

Clinics in Anaesthesiology. Current Topics in Intensive Care

By E. DOBB. Pp. 220. Bailliere Tindall, 1985. £16.25.

This issue contains contributions from Australian, American and United Kingdom experts who have provided a readable account of the various aspects of intensive care. The most useful chapters are those which describe the causes and management of failure of various organs. Acute hepatic failure is reviewed by Bihari, who stresses the high mortality of the condition and the frequency of associated encephalopathy, gastrointestinal haemorrhage, coagulopathy and renal failure. He recommends the administration of N-acetylcysteine up to 20 hours after severe paracetamol overdose, which is still the most common cause of fulminant hepatic failure. The use of mannitol to reduce elevations of intracranial pressure, correction of haemodynamic problems are stressed, as well as artificial liver support by means of haemodialysis, haemofiltration and haemoperfusion.

Thompson and Mansell describe the familiar problem of acute renal failure and Branthwaite reviews acute or chronic respiratory failure with her usual clarity and economy of words. The chapter entitled 'Alternatives to intermittent positive pressure ventilation', by Lawrence, is far more contentious. The suggestion is that most patients can breathe for themselves when managed with controlled airway pressure and possibly intermittent mandatory ventilation (IMV). This chapter is too dogmatic and uncritical, although it is interesting. The readers of this book have too much experience of ventilation of patients' lungs with, for example, chronic obstructive airways disease and of IMV to be told that IMV, from the moment of tracheal intubation, is 'the best method of management'. The other organ systems reviewed are the heart and circulation, the endocrine system and multiple system organ failure.

Clinics in Anaesthesiology starts slowly, with a description of stabilisation and transport of ill patients that seems to relate particularly to the Australian situation. Knaus and Zimmerman then discuss prediction of outcome from intensive care. The book ends with a summary of sedation and analgesia which is too patronising for most readers, who are likely to be experienced intensivists who use sedatives, analgesics and muscle relaxants with much thought and care.

The book is good in most parts and deserves to be purchased by hospitals with intensive care units.

R. GREENBAUM

Resuscitation. Care of the Critically Ill, 2nd edition

By D.K. BROOKS. Pp. 454. Edward Arnold, 1986. £72.50.

It is nearly 20 years since the first edition of this book was published. The second edition is expanded in size, scope and, inevitably, in price, but remains a single-author text which embraces a wide range of aspects of the care of the critically ill. These are covered in a quite astonishing degree of detail and it is this attempt by the author to represent authoritatively every aspect of this vast subject which proves his undoing.

The book starts well with a fascinating historical account of resuscitation, followed by a detailed and well-written chapter on fluids and electrolytes in health and disease, which includes more than 340 references (although many are purely of historical interest). These, and the succeeding two chapters on acid-base regulation and renal failure' respectively, are clearly the author's *forte*, although sometimes the intensity is overdone. Is it necessary, for example, to have on consecutive pages a graph *and* a detailed table for the conversion of pH to hydrogen ion concentration?

It is in the chapter on respiratory failure that one first senses that all is not well. Advice to institute intermittent positive pressure ventilation of the lungs in respiratory failure via a tracheostomy in preference to a tracheal tube, and to deflate the cuff of the tracheostomy tube at regular (unspecified) intervals hardly represents modern practice. And so it goes on—the chapter on shock contains much excellent material, particularly on the biochemistry of haemorrhagic and septic shock, and several pages on the measurement of central venous pressure, but hardly a mention of the technique or value of pulmonary artery flotation catheterisation. Occasionally the reader is startled by statements such as 'postural hypotension ... is becoming a very common condition in this era of addiction to television viewing'.

There are odd imbalances in the subjects covered. There are three and a half pages on the detailed management of lactic acidosis induced by phenformin (which the author justifies in the preface on the basis that this obsolete drug may still be taken by visitors from overseas), yet there is no mention of the emergency management of croup in children; nor, indeed, with the exception of formal tracheostomy, is there any mention of life-saving emergency techniques for relieving respiratory obstruction such as cricothyroid puncture and mini-tracheotomy.

It is particularly in some of the statements associated with anaesthesia that the weakness of single authorship is revealed. These range from misconceptions (the Ambu resuscitator is described as a 'rebreathing bag') and outdated advice (such as the use of methylamphetamine to reverse hypotension caused by thiopentone), to more bizarre recommendations such as the use of intramuscular (*sic*) pancuronium to overcome the muscle spasm of malignant hyperthermia. Some of the implied advice is dangerously misleading. For example, (following pulmonary aspiration of gastric contents) '... during the following 24 hours increasing respiratory dysfunction develops ... until the hypoxia is so severe that it may be incompatible with life. It *then* (my italics) becomes necessary to institute artificial respiration of the lungs and sometimes to perform a tracheostomy'.

This is a book of curious mixtures. Although much of it is excellent, and many working in the fields of resuscitation and intensive care will find much to interest and stimulate them, it cannot be recommended to trainees in anaesthesia who will be confused by the many unorthodox views presented. It is likely, though, that the price alone will deter most trainees from buying the book.

J.N. HORTON

Perinatal Anesthesia (Contemporary Issues in Fetal and Neonatal Medicine)

By J.W. SCANLON. Pp. 300. Blackwell Scientific Publications, 1985. £32.50.

This book is one of a series on contemporary issues in fetal and neonatal medicine. The title is misleading since the contents cover selected aspects of the effects of drugs (including anaesthetic agents) on the mother, fetus and neonate during pregnancy, not restricted to the perinatal period. The initial chapters are concerned with the effects of drugs administered during labour and delivery for pain relief, therapy for concomitant disease and self abuse by drugs. Anaesthesia and surgery in normal pregnancy are considered in detail and this is followed by an excellent and comprehensive chapter on maternal disease and anaesthesia.

Rather than the usual account of neonatal resuscitation, an illuminating chapter on neonatal anaesthesia is included. Not surprisingly in a book edited by an authority pre-eminent in the field of neonatal neurobehaviour, is a chapter which contains an extensive review of the subject. This serves to highlight the enormous gaps in our knowledge; despite the attention neurobehaviour has received in recent years its influence on subsequent childhood development is still largely unknown.

Regional anaesthesia for labour and delivery is considered very briefly and is confined, almost exclusively, to a description of how to perform the blocks. Little attention is paid to associated complications and their possible effects on the neonate. Fluid and electrolyte balance in normal pregnancy and the management of diabetic pregnancy are considered in some detail. Ketonuria, so carefully monitored during labour in the United Kingdom in the nondiabetic, is not discussed; admittedly little need be said other than to avoid active treatment with dextrose-containing solutions, but this could be emphasised. The final chapters are concerned with anaesthesia for delivery of the compromised fetus and a review of endorphins in obstetrics. Are oestriols still being measured to assess fetal welfare?

The editor of this type of volume faces a daunting challenge. The interests of different groups concerned with obstetrics and neonatology have to be stimulated without the offence of oversimplification or reiterating platitudes. The choice of subjects (or issues) will reflect the idiosyncrasies and enthusiasms of the editor, with the result that the selection may have neither a wide appeal nor reflect what the majority would consider to be current problems. This is, in my opinion, a successful, if not overwhelmingly so, attempt at overcoming these difficulties. Many of the contributors are not anaesthetists and while this is welcome, it is a little difficult to reconcile some suggestions with practical anaesthesia. If the fetus is compromised we are advised to avoid nitrous oxide and volatile agents until after delivery of the baby. Awareness is not considered. Surprisingly, the metabolic implications of nitrous oxide exposure are not discussed. It is easy to suggest subjects which are not included, but this is doing the book a disservice. It is not complete, but it does not purport to be a textbook; there is much in it which is neither available in a single source, nor readily accessible. It is well produced and edited. Its presentation is a challenge for the future and some comfort for the present, both of which I enjoyed.

J. THORBURN

Anaesthesia, 1986, Volume 41, pages 978–986

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for March 1986. The journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

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The collator of this section is Dr L. Kaufman, MD, FFARCS. Anaesthetic Office, The Rayne Institute, University College, University Street, London, WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data is held on Dbase II, and is available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address.

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Harvard Medical School, Associate Anaesthetist
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The Editor is grateful for the cooperation he has received in revising this information. It is believed to be accurate but those intending to attend a course should check the details with the relevant organiser. Applications and further information cannot be provided by *Anaesthesia*. These lists may not yet be complete, and it is hoped that information will be sent to the Editor to enable the necessary corrections to be made to keep them as up to date as possible.

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BIRMINGHAM			
Postgraduate Medical Centre, East Birmingham Hospital, Bordesley Green East, Birmingham, B9 5ST	7–9 October	£105	Postgraduate Secretary, Postgraduate Medical Centre, East Birmingham Hospital, Bordesley Green East, Birmingham, B9 5ST
Postgraduate Centre, Queen Elizabeth Hospital, Birmingham B15 2TH	2 September 1986 to 17 February 1987	£375	Board of Graduate Clinical Studies, The Medical School, Birmingham, B15 2TJ *Tel.* 021 472 1301 *ext.* 3317
DUNDEE			
Ninewells Hospital and Medical School, Dundee	September–March, Monday afternoons (followed by Part 2)	NO FEE	The Secretary, Department of Anaesthesia, Ninewells Hospital and Medical School, Dundee, DD1 9SY *Tel.* 0382 60111 *Ext.* 2175
EDINBURGH			
Department of Anaesthetics, Royal Infirmary, Edinburgh	Basic concepts in anaesthetic practice 5–9 January 1987 21–25 September 1987	FEE ON APPLICATION	The Secretary, Department of Anaesthetics, Royal Infirmary, Edinburgh, EH3 9YW
	In-service teaching, 1 session per week October–December 1986 April–May 1987 October–December 1987		As above
OXFORD			
John Radcliffe Hospital, Headington Oxford, OX3 9DU	3-day course in October and May (Limited numbers)		Miss Kay Bicknell, Administrative Assistant, Postgraduate Offices, John Radcliffe Hospital, Headington, Oxford, OX3 9DU

LONDON

Department of Anaesthetics, St Thomas' Hospital, London, SE1	5 September–7 November Day release, Fridays for 20 weeks	£185	Anaesthetic Course Secretery, St Thomas' Hospital, London, SE1 *Tel.* 01 928 9292 *ext.* 261
North London Hospitals' Course	11 September– 13 November 1986 20 November 1986– 5 February 1987 5 March–7 May 1987 14 May–16 July 1987 Thursdays—all day	£250	Course Office, Room 107, Rayne Institute, University Street, London, WC1E 6JJ *Tel.* 01 388 2411 *ext.* 242

SHEFFIELD

University Department of Anaesthetics	3–5 September Intensive course 25 September–27 November Thurday mornings		Mrs Broadhurst, Department of Anaesthetics, University of Sheffield, Beech Hill Road, Sheffield, S10 2RX

SOUTHAMPTON

Southampton General Hospital	Intensive Course 6–10 October 1986 12–16 January 1987 11–15 May 1987		Regional Postgraduate Administrator, Wessex Regional Health Authority, Highcroft, Romsey Road Winchester, SO22 5DH

SWANSEA

Postgraduate Centre, Morriston Hospital, Swansea, SA6 6NL	Alternate Mondays and Wednesdays in University term		Miss Jackett, Postgraduate Centre, Morriston Hospital, Swansea, SA6 6NL

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Pfizer Foundation, Edinburgh	Scientific Basis of Anaesthesia 12–16 January 1987 1–5 June 1987	FEE ON APPLICATION	Postgraduate Dean, Edinburgh Postgraduate Board for Medicine, Pfizer Foundation, Hill Square, Edinburgh, EH8 9DR *Tel.* 031 667 1011 *ext.* 4521/3
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LEEDS Leeds General Infirmary	September–July Alternate Wednesdays 3 × 13 week terms	NO FEE FOR THOSE EMPLOYED IN THE REGION	Departmental Secretary, Department of Anaesthesia, 24 Hyde Terrace, Leeds, LS2 9LN *Tel.* 0532 431751 *ext.* 6172
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MANCHESTER Withington Hospital, Manchester, M20 8LR	Day release (Wednesdays) 1 October–17 December 1986 7 January–25 February 1987	£280	Secretary for Advanced Courses, Department of Postgraduate Medical Studies, Gateway House, Piccadilly South, Manchester, M60 7LP
NEWCASTLE Royal Victoria Infirmary, Newcastle upon Tyne, NE1 4IP	Day release (Wednesdays) 24 September– 17 December 1986	NO FEE	The Secretary, Department of Anaesthesia Newcastle upon Tyne, NE1 4LP *Tel.* 091 232 5131
SHEFFIELD University Department of Anaesthetics	25 September–27 November, Thursday afternoons		Mrs Broadhurst, Department of Anaesthetics, Medical School, Beech Hill Road, Sheffield, S10 2RX
SOUTHAMPTON Southampton General Hospital	Intensive course 8–12 September 1986 23–27 March 1987		Regional Director of Postgraduate Studies, Wessex Regional Health Authority, Highcroft, Romsey Road, Winchester, S022 5DH
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CAMBRIDGE Addenbrooke's Hospital and Papworth Hospital	December 1986 and May 1987 3-day intensive revision course	£90	The Secretary, Anaesthetic Department, Addenbrooke's Hospital, Hills Road, Cambridge, CB2 2QQ

CARDIFF			
Department of Anaesthetics, University Hospital of Wales	Monday afternoons, January–May Day release	£90	Dr J. N. Horton, Department of Anaesthetics, University Hospital of Wales Heath Park, Cardiff, CF4 4XW
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Other courses

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The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

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Chapter in book

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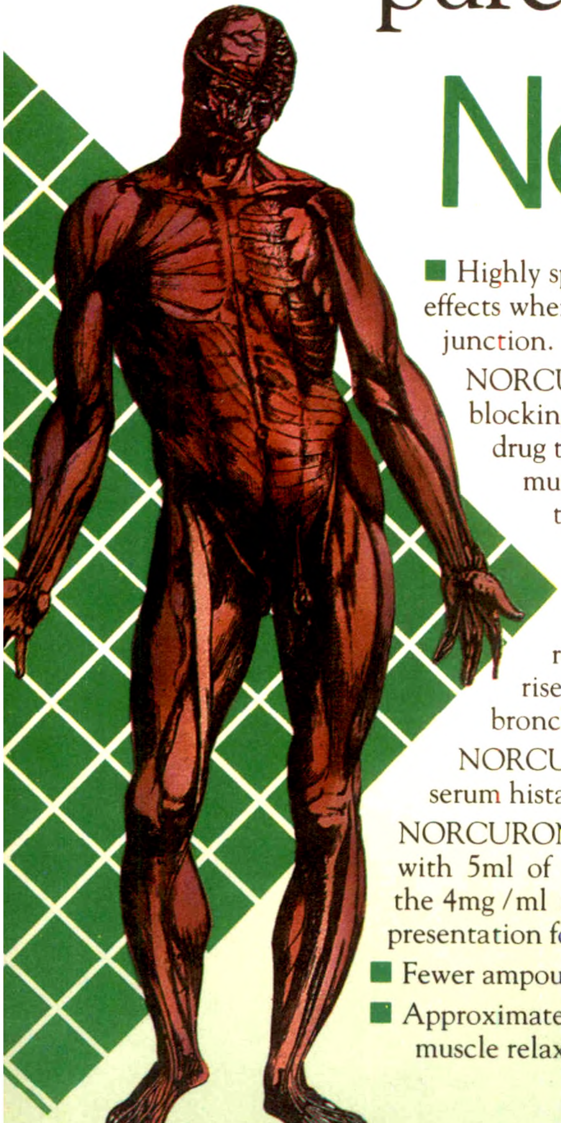

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Anaesthesia

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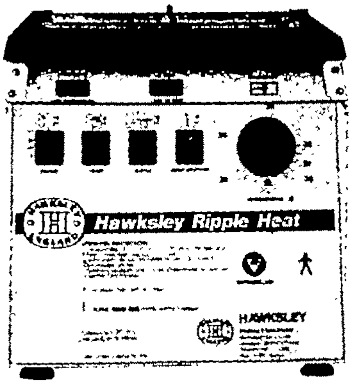

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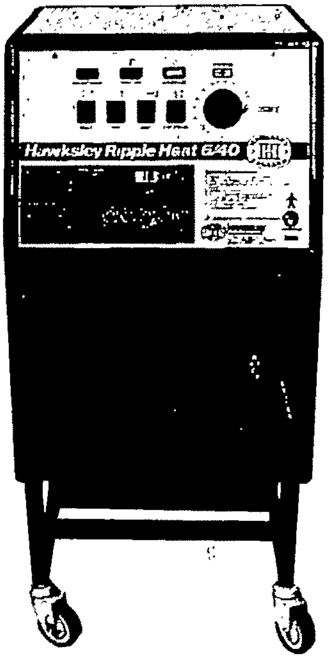

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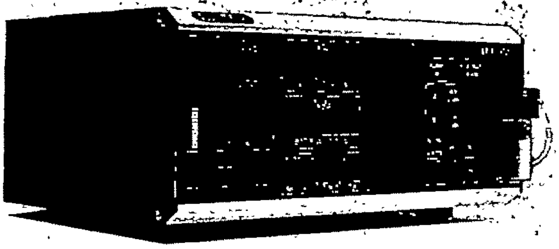

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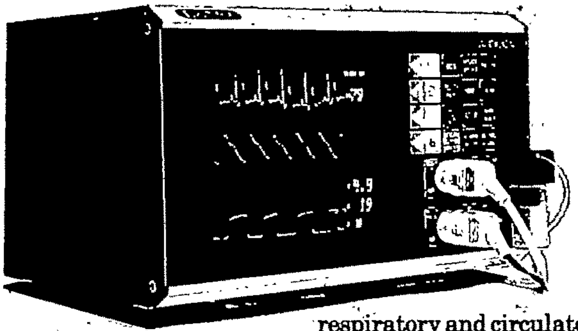

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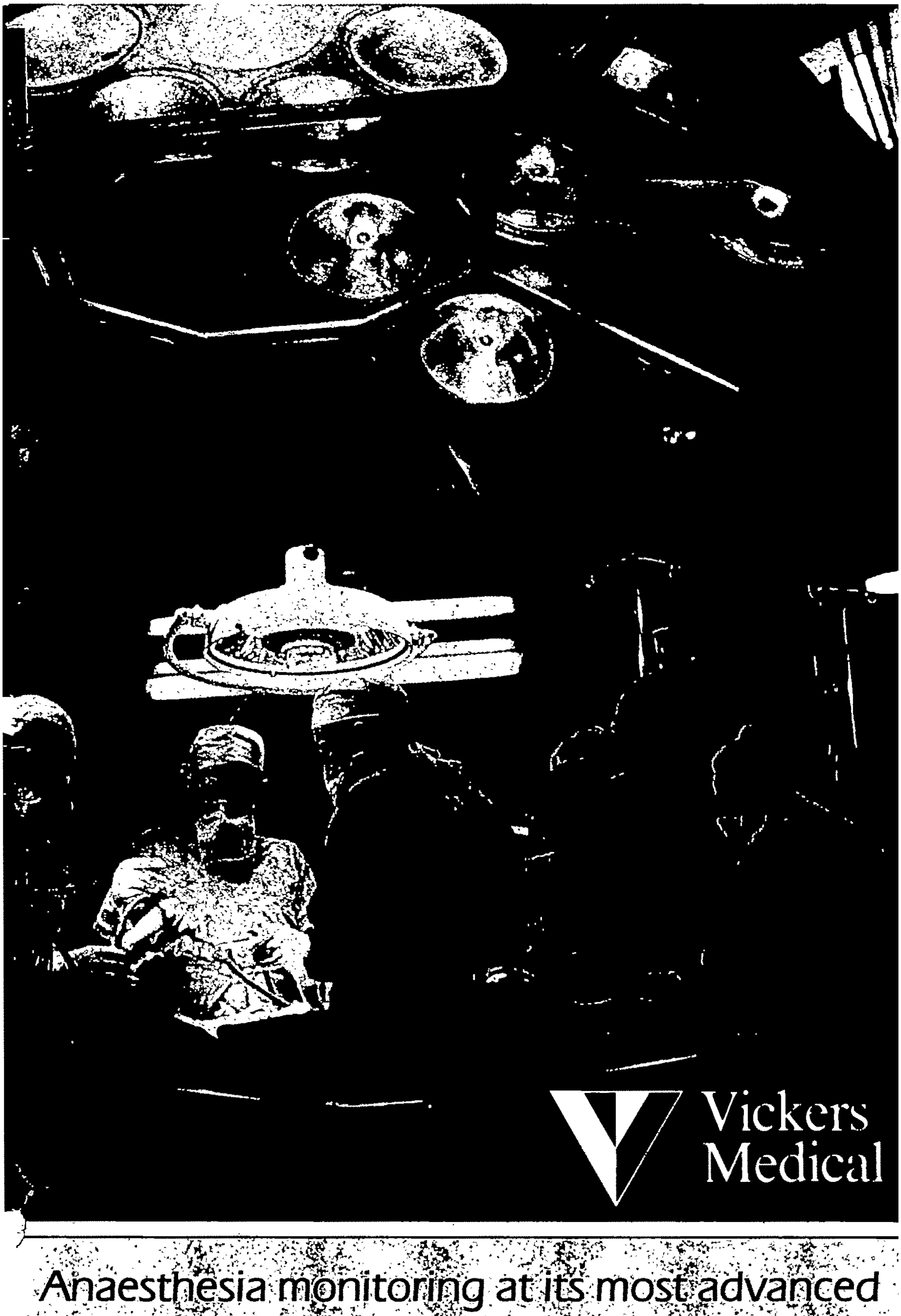
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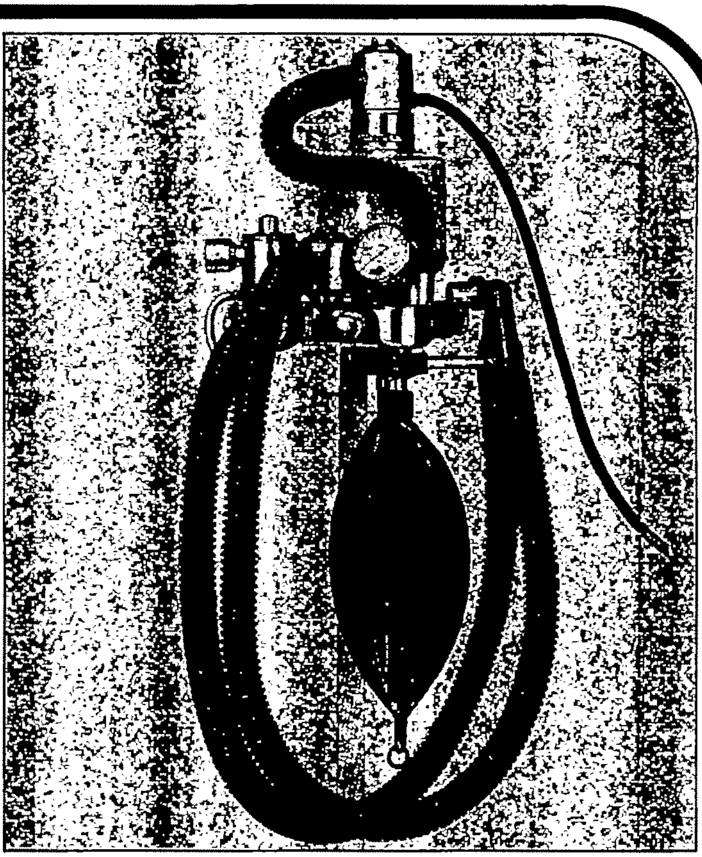

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Anaesthesia, 1986, Volume 41, pages 993–994

Editorial

Just more mountains to conquer

The Association of Anaesthetists of Great Britain and Ireland has attained a substantial objective on commissioning handsome premises at nine Bedford Square. A great effort has been required by Council, Officers and many members to maintain deadlines in construction and furnishing. The result is generally agreed as satisfactory. The generosity of members, industry and various trusts has helped the Association to succeed promptly in meeting the Appeal. The Association is doing well. There are solid grounds for self-congratulation, but there is always more to do and we must be prepared for new problems.

There is often a feeling that at large meetings there are insufficient opportunities for detailed discussion on specialised subjects in which perhaps only few may be interested and the solution is the workshop or seminar format. Our new headquarters are well suited to fill this gap in our educational schemes and can accommodate simultaneously three groups of up to 40 participants. Trial programmes, which are oversubscribed, have now been held to gauge enthusiasm and to test the facilities. Regular seminars will be arranged, starting in 1987, to enable members to have an opportunity to attend at least one workshop or seminar each year; these are planned to cover a large variety of subjects. The smaller size of the workshop, unlike the large national meeting which still serves an important function, should also ensure that departmental manpower is not strained. Any seminar of broad interest or with novel features will be published in full or in summary.

Professional status with the accompanying right to self-regulation must be safeguarded. To ensure this we must demonstrate to the public our willingness to engage in audit and to ensure high standards of practice. The Confidential Enquiry into Perioperative Death, now nearly complete, will teach us many new lessons and should point to important improvements in anaesthetic and surgical services. However, it would be more efficient to learn about inadequacies at an early stage. We therefore seek markers which can more rapidly point to inadequacies and a survey of anaesthetic accidents and near misses is being developed. This information could be exceedingly important in developing safer practices, in determining the value of relevant monitoring and ensuring that accepted principles are put into practice.

An ever-present problem is the irregular nature of Health Service funding for equipment. Most Departments of Anaesthetics have had negligible opportunities to plan budgets, which leads to major anomalies. It is obviously easier for an administrator to reduce or stop an equipment budget, than to terminate a marginally useful, or defunct service, an action which could save more money. Surging and ebbing equipment budgets make departmental planning impossible, deflate morale, and devastate industry. We must develop plans which can lead to more efficient budgeting for equipment and so to better use of resources. We must also ensure that these are disseminated effectively to Health Authorities.

In clinical practice, postoperative care is still grossly unsatisfactory. This problem could be substantially resolved by the fuller introduction of progressive patient care, especially the wider introduction of the High Dependency Unit. There are still difficulties in having this concept fully accepted, but logic must in the end prevail. This aim cannot be beyond the scope of a specialty which has already succeeded in implementing the recovery room and intensive care unit as part of every acute hospital.

Manpower planning is a perennial problem and we cannot move alone. Although anaesthesia has less serious problems than many other specialties, nevertheless, we must explore options that are suited to anaesthetic practice, which is a sharp end specialty. We wish to ensure a stable, flexible structure which brings together the essential elements of training, service and a satisfactory career, taking into account current political possibilities.

The academic departments of anaesthetics are the seed corn of the specialty. Their independence

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must be supported and we must try to ensure that they have resources to carry out their functions. There are serious problems at present, for instance in ensuring satisfactory careers, especially for the non-professorial staff. Resources are inadequate and earnings below National Health Service equivalents. This Association must see that the case for support for our comparatively small academic departments is heard, that the present situation is at least maintained and, as soon as possible, substantially improved. Few departments have ever been adequately funded and their duties have extended continuously, sometimes nearly to breaking point.

These are some of the problems anaesthetists face. There are others and there will be more. This Association exists to enable its members to serve the community and there is never a time for complacency. Our task can be compared to mountain climbing. There is no ultimate summit, just more mountains to conquer.

The President,
Association of Anaesthetists of Great Britain and Ireland,
9 Bedford Square,
London WC1B 3RA.

M. Rosen

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 12 December 1986 for April 1987, 13 March 1987 for July 1987 and 12 June 1987 for September 1987.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

Anaesthesia, 1986, Volume 41, pages 995–1000

Comparison of induction characteristics of four intravenous anaesthetic agents

J. S. C. McCOLLUM AND J. W. DUNDEE

Summary

The induction characteristics of thiopentone, etomidate and methohexitone have been compared to those of propofol (2,6 di-isopropyl phenol) in unpremedicated patients. Propofol 2.5 mg/kg caused significantly more hypotension, excitatory side effects and pain on injection at the dorsum of hand than thiopentone 5 mg/kg. However, with regard to the latter two sequelae, etomidate 0.3 mg/kg and methohexitone 1.5 mg/kg caused similar or more frequent upset. Propofol 2.0 mg/kg was equipotent with thiopentone 4.0 mg/kg in terms of successful induction of anaesthesia. Hypotension may contraindicate the use of propofol in the hypovolaemic or unfit patient.

Key words

Anaesthetics, intravenous; thiopentone, propofol, etomidate, methohexitone.

Propofol (2,6 di-isopropyl phenol), an emulsion preparation of the drug originally formulated in Cremophor EL, is at present undergoing clinical trials. It induces anaesthesia in young unpremedicated subjects in the dose range 2.0–2.5 mg/kg.[1] Thiopentone remains, over the 50 years since its first reported use in man, the most popular induction agent in current practice, despite instability in aqueous solution, occasional marked falls in blood pressure, and the laryngospasm or bronchospasm associated with its use. Methohexitone is the only other rapidly acting barbiturate commercially available in Britain and it has a limited use where a rapid recovery is desired. Etomidate, despite the effects of long term use,[2] or even of an induction dose,[3] on adrenocortical function, is claimed by some to have minimal deleterious effects on the cardiovascular system and, like methohexitone, has a limited use in clinical practice.

It is important to examine the new drug propofol, in relation to those currently available, under strictly comparable conditions and with the minimum of observers. In adequate doses all four drugs will induce anaesthesia in one arm–brain circulation time and are interchangeable as induction agents. The object of the present study was to compare the induction characteristics of comparable doses of the four induction agents.

Methods

The study, for which local medical ethical research committee approval had been obtained, was a randomised between-patient comparison carried out on 300 unpremedicated subjects. All were healthy, of either sex and conformed to physical status 1 or 2 of the ASA classification. They were scheduled for elective operations for which intravenous induction of anaesthesia was an ap-

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propriate technique. The doses given were considered to be equipotent, but as there was some doubt as to the appropriate dose of thiopentone and propofol, both were studied at two dose levels.

All injections were given over 20 seconds into a vein in the antecubital fossa, forearm or dorsum of hand and patients received one of the following: thiopentone 2.5%, 4.0 mg/kg; thiopentone 2.5%, 5.0 mg/kg; methohexitone 1%, 1.5 mg/kg; etomidate 0.2%, 0.3 mg/kg; propofol 1%, 2.0 mg/kg; propofol 1%, 2.5 mg/kg. Patients were given 67% nitrous oxide in oxygen for 2 minutes following injection, then inhalation or intravenous agents as required for the subsequent operation.

A number of observations were performed during induction. Patients were asked if their arm or hand was comfortable during injection and any sensation was recorded. Feelings of numbness, coldness, etc. were disregarded. The success of induction, i.e. loss of verbal contact within 1 minute of the end of injection for a minimum of 30 seconds was noted. Rapid lightening of anaesthesia before supplementary agents took over was also noted. The arterial blood pressure and heart rate were recorded prior to and 2 minutes after injection of the chosen drug. The presence of excitatory (hypertonus, spontaneous movement, twitching, tremor) or respiratory (cough, hiccough, laryngospasm) side effects were recorded. Apnoea was defined as absence of breathing for 30 seconds or longer. Its frequency and duration (if > 30 seconds) was noted. For periods greater than 1 minute, manual artificial ventilation was carried out.

An overall assessment of induction was made by the anaesthetist at the time according to a four point scale:[4] Grade 1, no complications; Grade 2a, slight complications not interfering with the course of anaesthesia; Grade 2b, complications interfering with the course of anaesthesia; Grade 3, totally unsatisfactory anaesthesia. The grades are the anaesthetist's impression of the induction made at the time and are not a summation of side effects. Grades 1 and 2a indicate an acceptable induction.

Statistical analysis was performed using Student's *t*-test, Chi square with Yates' correction or Fisher's exact probability test where appropriate.

Table 1. Mean (SD) ages and weights ($n = 50$)

Agent, mg/kg	Age (year)	Weight (kg)
Thiopentone, 4.0	37 (12.3)	62 (12.8)
Thiopentone, 5.0	33 (11.8)	62 (11.2)
Etomidate, 0.3	34 (10.0)	59 (11.0)
Methohexitone, 1.5	33 (11.5)	62 (10.1)
Propofol, 2.0	33 (12.0)	63 (8.8)
Propofol, 2.5	37 (12.2)	63 (12.3)

Results

The patients were broadly comparable with

Table 2. Successful inductions ($n = 50$)

Agent	mg/kg	Induced	Rapid lightening
Thiopentone	4.0	45	6
Thiopentone	5.0	50	5
Etomidate	0.3	50	0
Methohexitone	1.5	48	2
Propofol	2.0	45	5
Propofol	2.5	50	0

Table 3. Cardiovascular changes in patients in whom an adequate depth of anaesthesia was induced

			Systolic blood pressure decrease			Heart rate increase mean %
Agent	mg/kg	*n*	21–40 mmHg	>41 mmHg	Mean %	
Thiopentone	4.0	39	3	0	6	6
Thiopentone	5.0	45	7	3	10	9
Etomidate	0.3	50	4	0	5	3
Methohexitone	1.5	46	1	0	1†	24‡
Propofol	2.0	40	17	2	15	5
Propofol	2.5	50	17	5	17*	5

*$p<0.05$; †$p<0.01$; ‡$p<0.001$ compared to thiopentone 5 mg/kg.

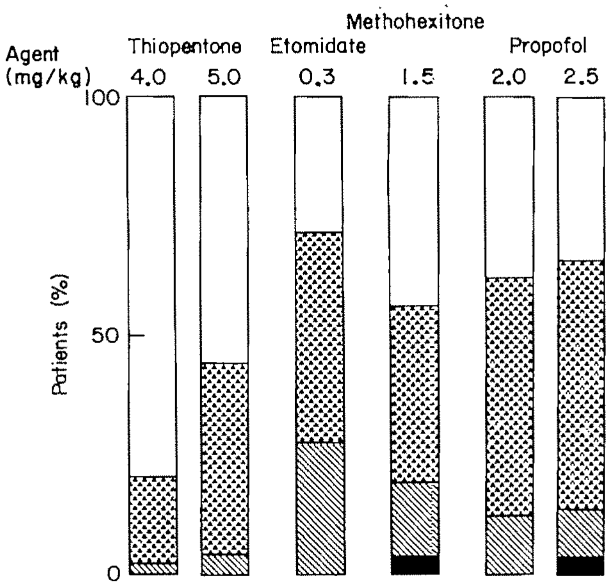

Fig. 1. Percent systolic blood pressure change from baseline in individual patients, with mean.
☐, Uncomplicated; ▩, mild upset; ▧, moderate upset;
■, completely unsatisfactory.

respect to age and weight in all six groups (Table 1).

Anaesthesia was successfully induced in all 50 patients with thiopentone 5 mg/kg, etomidate 0.3 mg/kg and propofol 2.5 mg/kg. Rapid lightening occurred in five patients receiving thiopentone 5 mg/kg. The other drugs/doses failed to induce all patients and again rapid lightening occurred (Table 2).

Thiopentone 4 mg/kg and etomidate had the least effect on blood pressure and heart rate (Table 3; Fig. 1). No patients who received these induction agents (or methohexitone) had a fall in systolic blood pressure of greater than 40 mmHg. In contrast, propofol 2.0 and 2.5 mg/kg caused more hypotension than thiopentone 5 mg/kg ($p = 0.07$ and 0.02 respectively). At 2 minutes, the mean fall in systolic pressure was 15% with propofol 2.0 mg/kg and 17% with 2.5 mg/kg. Heart rate rose slightly with all agents at 2 minutes; the largest change was with methohexitone (24% and $p < 0.001$ compared to thiopentone 5 mg/kg; Table 3).

Table 4 shows the incidence of excitatory and respiratory side effects in patients in whom an adequate depth of anaesthesia was induced. Thiopentone in both doses was significantly less excitatory than etomidate, methohexitone, propofol 2.0 mg/kg and propofol 2.5 mg/kg, although the extent of muscle movement with propofol was very small compared with methohexitone and etomidate. Methohexitone caused a

Table 4. Percent incidence of excitatory and respiratory side effects in patients in whom an adequate depth of anaesthesia was induced

Agent	mg/kg	*n*	Excitatory	Respiratory
Thiopentone	4.0	39	8	8
Thiopentone	5.0	45	9	9
Etomidate	0.3	50	70‡	10
Methohexitone	1.5	46	37†	20
Propofol	2.0	40	33†	5
Propofol	2.5	50	24*	6

*$p < 0.05$; †$p < 0.01$; ‡$p < 0.001$ compared to thiopentone 5 mg/kg.

Table 5. Number of patients exhibiting apnoea > 30 seconds

Agent	mg/kg	31–60 seconds	> 61 seconds
Thiopentone	4.0	10	1
Thiopentone	5.0	18	1
Etomidate	0.3	0	0
Methohexitone	1.5	9	1
Propofol	2.0	7	5
Propofol	2.5	16	6

Table 6. Percent incidence of pain at injection site

Agent	mg/kg	Antecubital fossa	Dorsum of hand
Thiopentone	4.0–5.0	4	5
Etomidate	0.3	14*	29‡
Methohexitone	1.5	18†	41‡
Propofol	2.0–2.5	8	31‡

*$p<0.05$; †$p<0.01$; ‡$p<0.001$ compared to thiopentone.

higher incidence of respiratory effects than any of the other drugs studied, none of which differed significantly in this respect.

Only propofol (Table 5) caused prolonged apnoea lasting more than 1 minute in more than one patient (11% of all patients studied). As defined in this study, apnoea was not seen in any patients receiving etomidate. The incidence of pain during injection reported following antecubital injection of propofol (Table 6), compares favourably with thiopentone and is higher with etomidate and methohexitone. With dorsum of the hand injection, the incidence of pain was unchanged with thiopentone but the other three drugs caused significantly more pain.

If unacceptable inductions due to failure and/or rapid lightening are excluded, thiopentone is still the smoothest induction agent of the four, with 96% acceptability (Fig. 2). Propofol was acceptable in 87% of cases; poorly graded inductions were due to cardiorespiratory depression. Methohexitone had an acceptability rate of 80% and etomidate 72%; severe excitatory or respiratory side effects caused the majority of problems.

Discussion

In this study we evaluated the induction characteristics of four agents. The ED_{95} of the current formulation of propofol has been estimated as 2.5 mg/kg.[1] However, in a previous study from this Department,[5] anaesthesia was reliably induced by 2.25 mg/kg in 97% of patients. Our results confirm that 2.0 mg/kg is an inadequate induction dose of propofol for fit unpremedicated adults. However, even this dose caused significantly more hypotension than thiopentone 5 mg/kg (Table 3). The greatest blood pressure fall was found in patients receiving propofol 2.5 mg/kg; the degree of fall was comparable to that reported by Fahy and colleagues.[6] In agreement with accepted views, etomidate proved to be a cardiostable induction agent. In contrast with the other drugs, methohexitone caused a significant rise in heart rate; this may explain its lesser hypotensive effect compared with thiopentone.

Excitatory phenomena were a marked feature of induction with methohexitone, etomidate and propofol; etomidate was the worst in this respect. Our incidence is similar to that reported by others.[7] In this study, 37% of patients receiving methohexitone showed excitatory effects; this was similar to the 33–34% found in previous studies.[8,9] Although propofol exhibits excitatory sequelae these were more mild and transient than those produced by the other two drugs and they are not a problem in clinical practice.

Propofol was remarkably free from respiratory side effects; only five out of 90 successfully induced patients showed any upset. This has been noted in a previous study.[10] Respiratory depression also appears to be a feature of propofol, but manual ventilation was easily tolerated in all cases until spontaneous respiration returned.

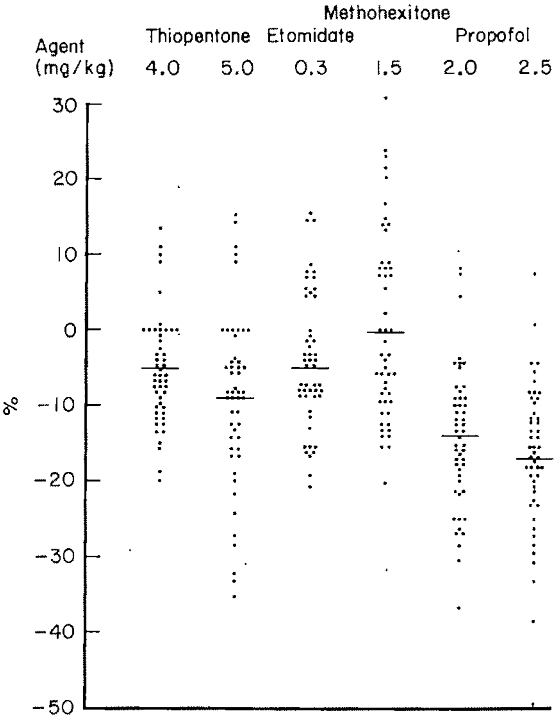

Fig. 2. Induction grades in patients in whom an adequate depth of anaesthesia was induced.

As noted by others, the incidence of injection pain varied markedly with site. Thiopentone caused least pain at both sites of injection, whereas methohexitone caused the most, even as a 1% solution. Our incidence with propofol and methohexitone is similar to that reported by others,[11-13] but we found less pain on antecubital injection with propofol than with either etomidate or methohexitone.

With regard to overall acceptability of induction to the anaesthetist, thiopentone scored highest with 96%, when failed inductions and/or rapid lightening were excluded (failed inductions scored 3 and rapid lightening 2b in our grading system). Propofol was more acceptable (87%) than either methohexitone (80%) or etomidate (72%) (the reduction with the latter two drugs was due to unwanted excitatory and respiratory side-effects). This is in contrast to propofol, where unacceptability was due mainly to marked cardiorespiratory depression.

In conclusion, propofol compares favourably with the other three induction agents in this study. It is superior to methohexitone and etomidate, causing less pain on injection and fewer side effects. The main problem concerning induction of anaesthesia with propofol is dose-related hypotension and this may preclude its use in elderly and hypovolaemic patients.

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Ro 15-1788 for postoperative recovery

A randomised clinical trial in patients undergoing minor surgical procedures under midazolam anaesthesia

J. WOLFF, P. CARL, T. G. CLAUSEN AND B. O. MIKKELSEN

Summary

In a double-blind randomised study, 100 women who underwent induced abortion under midazolam anaesthesia were given the benzodiazepine antagonist Ro 15-1788 or placebo after termination of anaesthesia. Recovery was assessed by means of a modified Steward coma scale. Following incremental doses of Ro 15-1788, 56% of the patients were fully awake within 3 minutes and 92% after 5 minutes, which was significant compared to the placebo group. The median duration of amnesia was 91 minutes after Ro 15-1788 compared to 121 minutes in the placebo group ($p < 0.001$)*. The median dose of Ro 15-1788 was 0.4 mg. A slight positive correlation between total dose of Ro 15-1788 and total amount of midazolam was found. Nausea and/or vomiting were found to be more frequent in the Ro 15-1788 group, but otherwise we found no differences between groups with regard to either side effects or cardiorespiratory function. Ro 15-1788 is evidently an effective antagonist to the sedation induced by midazolam.*

Key words

Hypnotics, benzodiazepines; midazolam.
Antagonists, benzodiazepines; Ro 15-1788.

The central pharmacological effects of benzodiazepines are considered to be mediated by facilitating the synaptic transmission of the inhibitory neurotransmitter γ-amino butyric acid (GABA).[1-3] Specific neuronal membrane receptors with high affinity to benzodiazepines have been demonstrated in the central nervous system,[4,5] and these receptors are thought to be coupled, at least in part, with the GABAergic synapses.[6]

Recently, the imidazodiazepine Ro 15-1788 (ethyl-8-fluoro-5.6-dihydro-5-methyl-6-oxo-4H-imidazo [1.5-a] [1.4]-benzodiazepine-3-carboxylate) has been shown to be a potent, competitive inhibitor of the specific binding of benzodiazepines at the receptor level.[7,8] Studies in human volunteers have shown that Ro 15-1788 potently antagonises the central effects of 3-methylclonazepam,[9] diazepam,[10] flunitrazepam,[11] and midazolam.[12] Only a few clinical trials, however, have dealt with the use of Ro 15-1788 in anaesthesia.[13,14]

The aim of the present study was to investigate the efficacy, safety and dose requirements of the benzodiazepine antagonist Ro 15-1788 for reversal of sedation and amnesia in the early

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recovery period following midazolam anaesthesia.

Methods

One hundred female patients (ASA 1–2) with a pregnancy of less than 12 weeks undergoing therapeutic abortion on an outpatient basis took part in this study. Patients were consecutive, but those with neurological disease, known allergy to benzodiazepines or who were receiving treatment with psychotropic drugs (including benzodiazepines) were not studied. The trial was conducted in accordance with the Helsinki II Declaration and approved by the local ethics committee. Informed consent was obtained from each patient before anaesthesia.

One hour before surgery the patients were premedicated with midazolam 7.5 mg orally. Anaesthesia was induced with midazolam 0.3 mg/kg intravenously, together with fentanyl 0.15 mg. A further dose of midazolam 0.15 mg/kg was administered if the eyelash reflex was still present 3 minutes after the initial dose. Anaesthesia was maintained with 67% nitrous oxide in oxygen. If necessary, supplementary doses of midazolam 0.15 mg/kg or fentanyl 0.05 mg, or both, were injected.

Immediately after termination of anaesthesia, patients were randomly assigned to one of two groups (A and B). Patients in group A ($n = 50$) received 0.2 mg Ro 15-1788 (0.1 mg/ml) intravenously and further doses of 0.1 mg intravenously at intervals of one minute until the maximum score on the modified Steward coma scale was obtained or a total dose of 1.0 mg had been given. In group B ($n = 50$) placebo (normal saline) was administered according to the same regimen. Treatments were administered under double-blind conditions.

Postoperatively, the patients remained in the operating theatre for 15 minutes and were then transferred to the recovery room. Altogether they were observed for 4 hours and discharged from hospital 6 to 8 hours after surgery. All postoperative observations were performed by the authors.

Recovery was assessed by means of a scoring system, first described by Steward,[15] and later modified by Robertson *et al.*[16] (Table 1). In the present study a score of 9 indicated complete recovery to the awake state. Assessment was performed at one-minute intervals for 15 minutes following termination of anaesthesia, then at 15-minute intervals for the next 225 minutes. Arterial blood pressure and heart rate were measured at the same intervals with a Sentry ASD 400 monitor (oscillometric method). Respiratory rate was recorded and arterial blood gas tensions analysed (ABL 2, Radiometer, Denmark) before anaesthesia, immediately before injection of Ro 15-1788 or placebo and 60, 120 and 180 minutes thereafter. All unwanted side effects were noted during the observation period. Signs of local reaction (pain, tenderness or erythema) at the injection site were recorded immediately after injection of Ro 15-1788 or placebo and after 60 minutes.

Table 1. Modified Steward coma scale. A score of 9 indicates complete recovery to the awake state

Consciousness	Score
Fully awake, eyes open, conversing	4
Lightly asleep, eyes open intermittently	3
Eyes open on command or in response to name	2
Responding to ear pinching	1
Not responding	0
Airway	
Opening mouth or coughing or both, on command	3
No voluntary cough, but airway clear without support	2
Airway obstructed on neck flexion, but clear without support on extension	1
Airway obstructed without support	0
Activity	
Raising one arm on command	2
Non-purposeful movement	1
Not moving	0

Before leaving the recovery room, patients were interviewed in order to estimate the duration of amnesia. A questionnaire was used to obtain information about specified complaints during the first 24 hours after surgery. The final question was whether or not the same type of recovery would be acceptable on a future occasion.

Statistical methods were Mann-Whitney and Chi square test for between-group comparisons. Differences in scores on the Steward scale, blood pressure, heart and respiratory rates and blood gases were evaluated by a non-parametric model[17] corresponding to analysis of variance for a 2-factor design with repeated measures on one factor. The significance level was 0.05.

Results

There were no significant differences between the

Table 2. Demographic data and duration of anaesthesia. Median (range)

	Ro 15-1788	Placebo
Age (years)	25.0 (18–44)	24.2 (18–43)
Weight (kg)	59.8 (47–89)	59.9 (45–76)
Height (cm)	167.3 (154–179)	169.0 (152–178)
Duration of anaesthesia (minutes)	11.6 (5–36)	12.1 (7–24)

Table 3. Dose requirements of anaesthetic agents. Median (range)

	Ro 15-1788	Placebo
Induction dose of midazolam (mg)	21.0 (15.0–32.0)	20.0 (13.5–26.0)
Maintenance dose of midazolam (mg)	18.0 (0–48.0)	13.6 (0–36.0)
Total dose of midazolam (mg)	36.5 (22.0–70.0)	33.0 (15.0–55.0)
Total dose of fentanyl (mg)	0.15 (0.1–0.2)	0.15 (0.1–0.2)

groups with regard to demographic data, duration of anaesthesia (Table 2) or dose requirements of anaesthetic agents (Table 3) ($p > 0.10$ in each case).

Following Ro 15-1788, the level of consciousness improved rapidly with a maximum score on the Steward scale after 6 minutes. Differences between the antagonist and placebo were already significant after 1 minute (median difference 0.6, 95% confidence limits 0.1–1.2). At 5 minutes the median difference was 5.4 (4.7–6.1) and at 75 minutes 0.30 (0.02–0.57). Thereafter, no significant differences between groups were demonstrated (Fig. 1).

No significant differences between groups in arterial blood pressure, heart rate, respiratory rate or arterial blood gas tensions were found. All values were within normal limits. Dose requirements of Ro 15-1788 are shown in Fig. 2. The median value was 0.4 mg (95% percentile range, 0.3–0.9 mg). All patients were awake within the dose range of 1.0 mg Ro 15-1788. A slight positive correlation between total dose of Ro 15-1788 and total amount of midazolam was found (Fig. 3).

Side effects are shown in Table 4. Nausea ($p < 0.05$) and vomiting ($0.10 > p > 0.05$) were more frequent following Ro 15-1788 than placebo. In most cases, however, these side effects were of short duration. No analgesics, anti-emetics or sedatives were administered during the recovery period. The only local reactions at the injection site were one case of erythema in each group.

All patients remembered receiving their premedication, and virtually all could recall induction of anaesthesia. However, only two patients (4%) in the Ro 15-1788 group and none in the placebo group were aware of their stay in the operating theatre during the first 15 minutes after surgery. The median duration of anterograde amnesia in the Ro 15-1788 groups was 91 minutes (range 11–201) compared to 121 minutes (range 59–223) following placebo ($p < 0.001$).

The questionnaire revealed that 91% in the Ro 15-1788 group and 90% in the placebo group would be satisfied with the same type of recovery again.

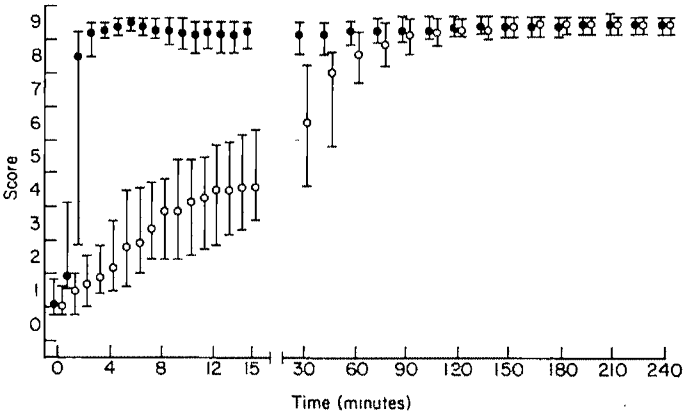

Fig. 1. Recovery scores on a modified Steward scale (0–9). ●, Values following Ro 15-1788; ○, placebo group. Median (interquartile range).

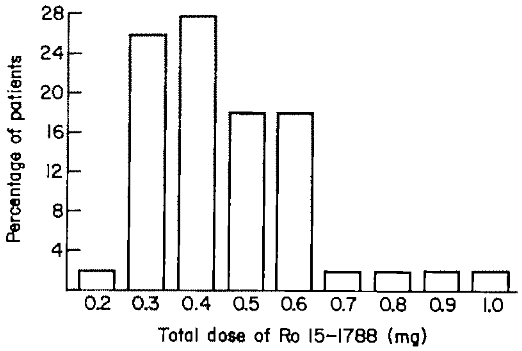

Fig. 2. Dose requirements of Ro 15-1788.

Discussion

The results of our study demonstrate that Ro 15-1788 is an effective antagonist for reversal of postoperative sedation after midazolam anaesthesia. Onset of action was prompt. After injection of incremental doses of Ro 15-1788 56% of the patients were fully awake within 3 minutes and 92% after 5 minutes. Recovery was assessed by means of a modified Steward scale. This scoring system emphasises the maintenance of a clear airway and the awake state, reflecting the essentials for patient safety. In our opinion, the system provided a sensitive

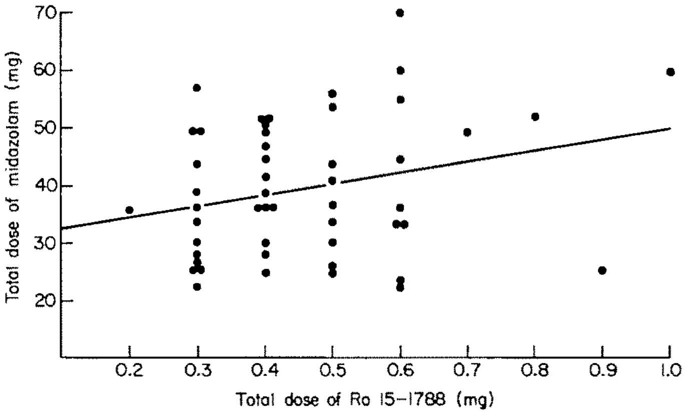

Fig. 3. Correlation between total dose of Ro 15-1788 and total dose of midazolam ($n = 50$), $r = 0.28$; $p = 0.0025$.

Table 4. Number of patients with unwanted side effects

	Recovery period		During the first 24 hours	
	Ro 15-1788	Placebo	Ro 15-1788	Placebo
Nausea	8 (16%)*	2 (4%)	9 (19%)	4 (9%)
Vomiting	7 (14%)	2 (4%)	5 (11%)	6 (14%)
Dizziness	0	0	15 (32%)	20 (47%)
Restlessness	0	0	6 (13%)	3 (7%)
Others				
Sweating	1 (2%)	0		
Headache	0	1 (2%)	2 (4%)	1 (2%)
Dysarthria	0	1 (2%)	0	1 (2%)
Fatigue	—	—	5 (11%)	8 (19%)
Insomnia	—	—	1 (2%)	0
Total no with side effects	8 (16%)	5 (10%)	27 (57%)	28 (65%)

*$p < 0.05$.

and reproducible method of estimating early postoperative recovery.

Pharmacokinetic studies have shown an elimination half life $(T_{\frac{1}{2}}\beta)$ of 0.9 ± 0.2 hours for Ro 15-1788.[18] This is in accordance with a brief duration of action of 1–3.5 hours.[12,19] In our study sedation did not recur. This might be attributed to the short sedation period after midazolam, as shown by the placebo group.

The anterograde amnesic action of midazolam was significantly attenuated following Ro 15-1788, although the difference is scarcely of clinical significance. No comparative data are available, but the amnesic properties of diazepam 20 mg were abolished, at least in part, with concommitant oral administration of Ro 15-1788 200 mg.[20] It is possible that higher doses of Ro 15-1788 in our study might have resulted in a more complete reversal of amnesia.

The median dose of Ro 15-1788 was 0.4 mg (95% percentile range, 0.3–0.9 mg). These findings suggest that the dose requirements for reversal of sedation following midazolam anaesthesia are much lower than those used in other investigations.[12,13] There was only a slight correlation between total dose of midazolam and total dose of Ro 15-1788, which means that the required reversal may be obtained by a fixed dose of Ro 15-1788, irrespective of the total amount of midazolam administered.

The lack of changes in the measured cardiopulmonary variables is in accordance with another investigation.[21] Number and nature of unwanted side effects following Ro 15-1788 were comparable with the placebo group, although nausea and vomiting were observed more frequently following Ro 15-1788. No serious side effects were registered. The previously described anxiety reactions following higher doses of Ro 15-1788,[21,22] indicating a possible intrinsic inverse action, were not observed in our study. However, a residual anxiolytic effect of midazolam and fentanyl cannot be excluded.

In conclusion, Ro 15-1788 seems to be an effective antagonist of sedation following midazolam anaesthesia, with only minor possible adverse effects. Amnesia was only abolished to a minor degree. The future role of Ro 15-1788 in anaesthesia might be comparable to that of the opioid antagonist naloxone.

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One-lung ventilation

The effect of positive end expiratory pressure to the nondependent and dependent lung

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Summary

We applied positive end expiratory pressure to the nondependent, nonventilated lung, or both nondependent and dependent, ventilated lung during one lung anaesthesia, and compared the results to those obtained by other techniques, such as increasing the inspired oxygen concentration in the dependent lung, or insufflating with oxygen using positive end expiratory pressure in the nondependent lung. Our study suggests that arterial oxygenation and intrapulmonary shunt can be lessened during one lung ventilation by continuous oxygen insufflation of the nondependent lung at 0.98 kPa positive end expiratory pressure while the dependent lung is ventilated with 0.49 kPa positive end expiratory pressure.

Key words

Anaesthesia; thoracic.
Ventilation; positive end expiratory pressure, shunt.

One lung ventilation using a double lumen bronchial tube provides good surgical exposure and prevents obstruction in the dependent lung due to either secretions or blood which might gravitate from the operated lung into the opposite dependent lung. However, one lung ventilation has often been associated with hypoxaemia, usually as a result of the increase of intrapulmonary shunt in the operated nondependent lung.

To minimise arterial hypoxaemia during one lung ventilation, many techniques have been employed; increased tidal volume,[1] positive end expiratory pressure (PEEP) to the dependent or nondependent lung,[2,3] high concentrations of inspired oxygen[4,5] and occlusion of the pulmonary artery.[6]

The present study compares the effect of PEEP in the nondependent lung, the dependent lung or both to prevent hypoxaemia during one-lung ventilation, with those obtained by other techniques.

Materials and methods

Seven patients who underwent lobectomy were studied. They ranged in age from 47 to 77 years. Informed consent was obtained from each patient pre-operatively. All patients were premedicated with 0.5 mg of atropine and hydroxyzine hydrochloride (50–100 mg) given intramuscularly.

Anaesthesia was induced with thiopentone (200–300 mg), after which 1 mg/kg of suxamethonium was given to facilitate intubation with a Carlen's or Robertshaw double lumen tube. The correct position of the tube was confirmed by

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auscultation before and after the patient was placed in the lateral position. Anaesthesia was maintained with 1% enflurane in 50% oxygen and nitrous oxide. Pancuronium bromide was used intermittently as needed for relaxation. Ventilation was maintained at a constant rate 12–15/minute (Servoventilator, Manley) and at a constant tidal volume of 10 ml/kg throughout the experiment.

Continuous oxygen insufflation and PEEP to the nondependent lung were performed using another anaesthetic machine. Continuous PEEP in the system was maintained and adjusted manually by using the pressure relief valve. The PEEP valve was connected to the expiratory limb to deliver PEEP to the dependent lung.

In seven patients, the following procedures were sequentially performed in each patient. Two lung ventilation at a tidal volume of 10 ml/kg was carried out with zero end expiratory pressure (ZEEP) in the lateral position before the chest was opened (step 1). The upper lung was deflated to atmospheric pressure and the dependent lung was ventilated with ZEEP at the same tidal volume as the two-lung ventilation (step 2). The upper lung was insufflated with 0.98 kPa PEEP and the dependent lung was ventilated with 0.49 kPa PEEP (step 3). The upper lung was insufflated with 0.98 kPa PEEP and the lower lung was ventilated with ZEEP (step 4). The upper lung was opened to atmospheric pressure to permit collapse of the operated lung and the dependent lung was ventilated with 100% oxygen and ZEEP with the same tidal volume and rate (step 5). Two lung ventilation in the lateral position was carried out after the chest was closed (step 6).

Before induction of anaesthesia, a 22-gauge indwelling cannula was inserted into the radial artery under local anaesthesia. A balloon-tipped, flow-directed pulmonary artery catheter was inserted into the pulmonary artery through the internal jugular vein after induction of anaesthesia.

The alveolar–arterial oxygen tension gradient, $(A - a)DO_2$ and the intrapulmonary shunt $(\dot{Q}s/\dot{Q}t)$ were calculated using the standard shunt equation.[7] Every 20 minutes after initiating each step, radial and pulmonary arterial blood samples were obtained and analysis was performed immediately using a Radiometer ABL-2 blood gas analyser.

The above data were analysed using analysis of variance and Student's *t*-test; $p < 0.05$ was considered statistically significant.

Results

The mean Pa_{O_2} decreased significantly and $(A - a)DO_2$ and $\dot{Q}s/\dot{Q}t$ increased significantly when ventilation was changed from two lung to one lung ventilation and the upper lung was deflated to atmospheric pressure after thoracotomy, as shown in Table 1 (step 1 to 2).

The simultaneous application of 0.98 kPa PEEP with continuous oxygen insufflation to the upper lung and 0.49 kPa PEEP to the lower lung caused a significant rise in Pa_{O_2} and a significant decrease in $(A - a)DO_2$ and $\dot{Q}s/\dot{Q}t$. The application of PEEP to only the upper, nondependent, lung (step 4) also significantly increased the Pa_{O_2} and decreased $(A - a)DO_2$ and $\dot{Q}s/\dot{Q}t$ compared to one lung ventilation (step 2). However, arterial oxygenation was optimised more effectively with the application of PEEP to both lungs in step 3 compared with application to only the upper lung in step 4. Comparison of the values obtained when the inspired oxygen concentration was 100% (step 5) to previous values with 50% oxygen (step 2), ventilation of the lower lung showed a small but significant ($p < 0.05$) rise in Pa_{O_2} and a significant reduction in $\dot{Q}s/\dot{Q}t$.

Discussion

One lung ventilation of the dependent lung with atelectasis of the upper lung caused a significant reduction in Pa_{O_2} concomitant with an increase in $(A - a)DO_2$ and $\dot{Q}s/\dot{Q}t$, as reported by other investigators.[8,9]

Several mechanisms are thought to be involved in the development of the arterial oxygen desaturation during one lung ventilation. The main cause is perfusion of some proportion of pulmonary blood through the upper collapsed lung. Acute collapse of the lung does not reduce the blood flow through the atelectatic lung, therefore intrapulmonary shunting is increased.[10] However, the mechanism of hypoxic pulmonary vasoconstriction (HPV)[11,12] has been reported to improve oxygenation by redistributing the blood flow from the nondependent lung to the dependent lung. In animals, the effect of HPV in increasing pulmonary vascular resistance in response to acute atelectasis is maximal after 60 minutes and stable thereafter in the open chest.[11]

Table 1. Cardiopulmonary data during two lung and one lung ventilation. Mean (SE)

	TLV	UL deflated LL ZEEP ventilated	UL $PEEP_{10}$ insufflated LL $PEEP_5$ ventilated	UL $PEEP_{10}$ insufflated LL ZEEP ventilated	UL deflated LL 100% O_2 ventilated	TLV
Step	1	2	3	4	5	6
Pa_{O_2} (kPa)	29.6 (3.8)*	14.3 (3.4)	28.6 (3.3)*	26.1 (3.8)*	16.0 (2.9)	27.6 (2.6)*
Pa_{CO_2} (kPa)	4.8 (0.16)	4.3 (0.25)	4.0 (0.40)	4.0 (0.28)	3.9 (0.33)	3.6 (0.26)
$(A-a)D_{O_2}$ (kPa)	11.9 (4.6)*	27.9 (3.5)	16.1 (4.8)*	19.3 (5.2)*	28.0 (3.5)	16.8 (4.3)*
$\dot{Q}s/\dot{Q}t$ (%)	10 (4.1)*	29 (5.8)	10 (5.3)*	12 (2.9)*	13 (3.4)*	11.2 (3.6)*
BP (mmHg)	134 (9.0)	139 (5.2)	133 (13.8)	136 (7.7)	137 (13.6)	134 (8.0)
HR (beats/minute)	83 (12.0)*	101 (18.2)	95 (6.5)	116 (16.7)	80 (9.6)	96 (15.9)

TLV: two lung ventilation; UL: upper lung; LL: lower lung; ZEEP: zero end expiratory pressure; PEEP: positive end expiratory pressure; $PEEP_5$: 0.49 kPa PEEP; $PEEP_{10}$: 0.98 kPa PEEP; BP: systolic blood pressure; HR: heart rate (beats/minute).

*Shows significant difference compared with step 2 ($p < 0.05$).

The degree of HPV is modified by the action of anaesthetics. Inhalation anaesthetics such as halothane and enflurane have been reported either to inhibit or preserve HPV.[13,14] Intravenously administered ketamine and fentanyl appear to preserve HPV.[15] Therefore, these intravenously administered drugs may be beneficial to patients undergoing thoracotomy with one lung anaesthesia. However, Rees *et al.* reported that ketamine was not superior to enflurane anaesthesia in terms of arterial oxygenation during one lung anaesthesia.[15]

The present study was undertaken to compare pulmonary gas exchange using several techniques reported recently, especially the effect of PEEP during one lung anaesthesia. In step 4, the oxygen insufflation of the nondependent lung with PEEP resulted in significantly reduced $\dot{Q}s/\dot{Q}t$ and improved arterial oxygenation, compared to step 2 as reported by others.[2,3] The application of PEEP to both lungs in step 3 further improves Pa_{O_2} compared to step 4 (the application of PEEP to only the nondependent lung).

The effects of selective application of PEEP to the dependent lung on oxygenation is controversial. Brown *et al.*[16] ventilated patients with selective PEEP to the dependent lung while ventilating the nondependent lung at ZEEP in the lateral position during thoracotomy; this ventilation method resulted in adequate arterial oxygenation with 30–50% inspired oxygen. However, some studies have reported that the application of PEEP to the dependent lung did not maintain adequate arterial oxygenation.[17]

The application of 0.49 kPa PEEP to the dependent lung during collapse of the nondependent lung decreased arterial oxygen tension[3,17] or did not change it.[18] Capan *et al.*[3] used differential lung ventilation similar to our procedure, with the dependent lung ventilated with 0.98 kPa PEEP while insufflating the nondependent lung with continuous oxygen at 0.98 kPa. Contrary to our findings, these manoeuvres did not optimise arterial oxygenation unlike ventilation of the dependent lung with ZEEP. One explanation for this discrepancy is that we ventilated the dependent lung with comparatively low PEEP (0.49 kPa); therefore, the low PEEP did not adversely affect the pulmonary haemodynamics.

On the other hand, the higher PEEP to the dependent lung, which Capan *et al.* used, may have decreased cardiac output secondary to impairment of venous return and increased pulmonary resistance caused by the compression of the intra-alveolar vessels due to the PEEP-induced increase in lung volume. The increase in pulmonary resistance with higher PEEP also diverted blood flow away from the dependent lung to the nondependent lung; this resulted in an increase of the intrapulmonary shunt in the nondependent atelectactic lung.

During thoracic surgery in the lateral position, the atelectasis in the dependent lung might be produced by mediastinal shift towards the dependent lung by gravity, and compression of the abdominal contents due to paralysis of the diaphragm. In the lateral position, the blood also flows predominantly to the lower dependent lung to result in decreased ventilation.[19] These combined factors reduce lung volume in the dependent lung and also cause the maldistribution of ventilation and perfusion; this leads to reduced Pa_{O_2}, increased alveolar–arterial O_2 differences and increased intrapulmonary shunt. Therefore, to prevent atelectasis and airway closure, some positive end expiratory pressure is required to expand the collapsed alveoli in the dependent lung, because PEEP causes an increase in lung volume at end expiration and thereby, an increase in functional residual capacity.

Techniques other than the application of PEEP have been investigated to improve arterial oxygenation. Increasing the tidal volume at constant respiratory frequency of the dependent lung did not improve arterial oxygenation.[1] The use of high inspired oxygen concentration in the dependent lung also did not prevent a fall in Pa_{O_2} when the nondependent lung was deflated to atmospheric pressure.[4]

Pneumonectomy and even lobectomy, which reduce the blood flow through the atelectatic lung, significantly improved arterial oxygenation.[5] Alfery *et al.*[6] showed in an animal study that inflation of a balloon positioned in the main pulmonary artery of the nondependent lung improved Pa_{O_2}, and diverted blood flow to the ventilated lung. Therefore, ligation or clamping of the nondependent lung pulmonary artery as early as possible is a useful technique to reduce the shunt blood flow through the nonventilated lung and to improve the arterial oxygenation.

The present study suggests that the application of PEEP to both nondependent and dependent lung is a useful technique for improving arterial oxygenation and reducing intrapulmonary shunt during one lung ventilation.

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AIDS and anaesthesia

K. G. LEE AND N. SONI

Summary

The Acquired Immune Deficiency Syndrome (AIDS) is a group of conditions which is reaching epidemic proportions. It is caused by a virus new to man, with an as yet poorly understood natural history, ominous prognosis and no known cure. Anaesthetists should be aware of the implications of dealing with increasing numbers of both diagnosed and undiagnosed AIDS patients and asymptomatic carriers in the fields of resuscitation, intensive therapy and theatre anaesthesia. The misunderstanding of AIDS is as extensive as the literature on the subject and a review of the current knowledge of the disease relevant to the anaesthetist is pertinent.

Key words

Acquired Immune Deficiency Syndrome.

The Acquired Immune Deficiency Syndrome (AIDS) is defined by the Centers for Disease Control (CDC Atlanta, Georgia, USA) for the purposes of epidemiological study as: 'A reliably diagnosed disease that is at least moderately indicative of an underlying cellular immune deficiency. For example, Kaposi's sarcoma in a patient less than 60 years, or opportunistic infection ... No known underlying cause of the cellular immune deficiency nor any other cause of reduced resistance reported to be associated with the disease'.

This group of conditions was first observed in previously healthy homosexuals in New York and California in 1981, who suffered particularly from the rare malignancy, Kaposi's sarcoma, and opportunistic pneumonia caused by the protozoan *Pneumocystis carinii.* It was subsequently realised, however, that the spectrum of disease caused by the 'AIDS virus' is much greater than that covered by the CDC definition. Despite the extraordinarily rapid acquisition of knowledge of the syndrome in recent years, many fundamental questions remain unanswered, particularly those concerning its ease of spread and the nature and duration of its asymptomatic carrier state.

Current knowledge

AIDS is now known to be caused by a retrovirus of the subfamily Lentivirinae,[1] other members of which are known to cause lethal slow virus diseases in several animal species. The virus is thought to have crossed the species barrier from an African Green Monkey, in which it is harmless, to man in the same way as the viruses causing Lassa fever and Marburg disease. This virus is variously known in the literature as the lymphadenopathy associated virus (LAV), the AIDS-associated retrovirus (ARV) and the human T-

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cell lymphotropic virus type III (HTLV III). AIDS cannot occur without infection with this virus and infection with the virus is potentially lethal to man, irrespective of race, age, sex, life style or sexual practice.

A few weeks after infection the virus commonly causes an acute illness of short duration similar to glandular fever or influenza,[2] followed by an asymptomatic period lasting months or years. This may progress to a state of persistent generalised lymphadenopathy (PGL), weight loss, intermittent fever and diarrhoea, possibly with progressive encephalopathy.[3] Alternatively, progression may be to a more sinister state of immune deficiency, leading to the development of otherwise unusual malignancies such as Kaposi's sarcoma and non-Hodgkin's lymphoma, and severe opportunistic infections such as atypical pneumonias, tuberculosis, candidiasis and viral infections such as herpes.

The virus persistently infects a small minority of mature T-helper lymphocytes in peripheral blood, lymph nodes and spleen and it also persistently infects cells throughout the brain. It slowly replicates and is cytopathic to those cells in which it replicates, but it is not oncogenic in its own right like the other retroviruses known to cause leukaemia in man, HTLV I and II. The number of T-helper cells decreases and the ratio of T-helper to T-suppressor cells is reduced; this results in a degree of immune deficiency.[4] The slow cytopathic effect on the brain cells seems irreversible, but may take years to become clinically manifest. It may not show itself in most AIDS cases seen at present, since the immune deficiency is more immediately devastating. The average life expectancy in one USA centre from the first hospitalisation for opportunistic infection was 224 days.[5] Although infection and malignancy may to some extent be controlled, no therapeutic intervention has so far reversed the immune deficiency.[5]

Transmission of the AIDS virus, like that of hepatitis B, is by blood and semen, and it is likely that even a single virus particle will readily transmit the disease.[6] Both are thus easily transmitted by anal intercourse, due to mucosal injury. The virus is also transmitted by vaginal intercourse,[7] although the degree of intimate sexual contact needed for transmission is not known.[5] Both viruses are transmitted by needle injuries and contamination of cuts, sores and abrasions with the blood or serum of carriers. Transmission of AIDS by contact with saliva, by airborne droplets or by contamination of intact mucous membranes is unlikely, but has not yet been disproved.

The full range of incubation periods between infection and symptoms cannot yet be determined, as the upper limit exceeds the period which has elapsed since cases were first reported. The eventual mortality of AIDS may not be ascertainable until recently infected carriers are studied into the twenty-first century. It is not known how long the carrier state lasts, although it is likely to be for life, as in the case of hepatitis B. It is not known if all carriers will progress to frank AIDS or whether some remain asymptomatic. In the studies so far carried out, 4–19% of seropositive patients have progressed to AIDS over periods of 1–5 years. The existence of trigger mechanisms causing carriers to progress to AIDS has not been demonstrated. It is unclear whether asymptomatic carriers are more or less infectious than those with overt disease. AIDS may be less infectious than hepatitis B.[8]

In lentivirus infections in animals, preventative vaccine production has been impossible because of the variety and changes of antigenic strains found and the inability of the host to clear virus from the circulation. Similar difficulties might be expected with AIDS.[6]

Testing for HTLV III

The pattern of changes occurring in the ratio of suppressor T-cells to helper T-cells has already been discussed. Prior to the development of more specific tests for this virus, the use of this ratio enabled identification of people with atypical pneumonias who may fall into the category of having AIDS. Obviously this test was very non-specific and these changes in T-cell ratios can occur in other conditions. However, a variety of new tests have been developed which identify the antibody to HTLV III.

The enzyme linked immunosorbent assay (ELISA) is a test which is available commercially from several companies. It can be done relatively rapidly, in 2–3 hours, and may easily be carried out in the hospital laboratory. However, there are problems with the number of false positives that may be determined with this assay and current recommendations are that this test should be repeated at a reference laboratory for true confirmation. People particularly prone to develop false positive results are those who have had previous transfusions or multiparous women.

An electrophoretic technique (Western Blot) is designed to identify antibodies to proteins of specific molecular size. It is a very time consuming, labour intensive test which may take up to 2 weeks to produce results. Consequently, whilst it is not readily adapted for routine hospital use, it may be used as a confirmatory test in the reference laboratory.[9,10]

At the present time, although under certain special circumstances the virus may be identified in the laboratory, there is no easy test for either the virus or its antigen. This means that, in effect, there will always be potential for false negative results with the current antibody tests, as there will be a population of patients who, whilst having been exposed to the virus and having the virus in their circulation, have not yet developed the antibodies to the virus. This problem will remain until such time as an antigen test is available. These then are the tests that are currently available for HTLV antibodies and, while there are certain significant shortcomings in their ability to detect the virus or infection with the virus, the use of these tests for screening has significantly reduced the risk of HTLV III both in the area of blood transfusions and also in clinical practice.

Blood products

The development of HTLV III infection from blood transfusion and blood products has caused considerable anxiety. The incidence of the virus in the blood donor population will vary considerably from city to city and country to country, and figures of 1:500 have been quoted in some series.[11] The introduction of HTLV III antibody screening for all blood donors allows the use of more intensive questioning of blood donors, and the education of the population as a whole, should result in a significant reduction in the risk of transmission of HTLV III through either blood or blood products. As some of the pooled products that are used from Blood Transfusion Centres may involve large quantities of serum, the risk in these groups may still be present. This is particularly important with Factor VIII, which has been associated with a rather significant increase in seroconversion in several populations of haemophiliacs.[12] There are a variety of ways of treating human blood products which will immobilise the virus. For Factor VIII, dry heat may be used and, although this will produce a reduction in the efficacy of the Factor VIII and in the total quantity, it is effective in immobilising HTLV III. Other methods of inactivation such as alcohol precipitation or pasteurisation, whilst useful for sterilising albumin, will significantly alter the properties of the coagulation factors and are not, therefore, appropriate. The use of heat treatment in Factor IX is not so clearly delineated, although this product is now commercially available. Other blood products, including hyperimmune globulin, immunoglobulin and antithrombin 3 are all fairly rigorously pretreated and any HTLV III present is almost certainly inactivated. However, plasminogen, fibrinogen and other human tissue products may still be considered potentially hazardous.

When blood transfusions or the use of blood products is being considered, the anaesthetist is always aware of the potential transmission of agents such as hepatitis B, non-A, non-B, and cytomegalovirus. HTLV III is a new transmissible agent to be added to this list. The potential presence of HTLV III is obviously not an absolute contraindication to the use of blood products, but rather serves as a useful reminder that there is a definite morbidity associated with the transfusion of these products. Those individuals who are at risk of carrying HTLV III are listed in Table 1.

Table 1. Patients at risk of carrying HTLV III

Homosexuals/bisexuals
Intravenous drug abusers
Haemophiliacs
Female sexual partners of men at risk
Children of affected mothers
Patients of Haitian or Central African origin

Risk to the anaesthetist

In studies carried out so far, risk to health personnel seems low,[8,10,13] but transmission by needlestick injury with contaminated sharps has been implicated in cases of AIDS in hospital workers.[14,15]

Operating theatre

Asymptomatic patients with positive serology and patients with overt forms of the disease should both be managed in the same way in view of our current knowledge. At the pre-operative visit, there is no risk from casual contact. Precautions are advisable, however, if the patient is suffering from frank haemorrhage from any cause. The risk from body fluids such as sputum or urine is less clear, but it is recommended that they should be treated as potentially harmful. Patients with overt AIDS will probably already be nursed in isolation. Precautions recommended are the covering of clothing with a disposable apron or gown and the wearing of gloves. Recommendations also include the use of eye protection. In the case of the severely immunocompromised patient, 'reverse barrier' techniques to reduce the spread of infection to the patient may be indicated.

On transfer from the ward to the operating theatre there is no need for the patient to wear special clothing, mask, etc, routinely unless the patient is suffering from gross expectoration, haemoptysis or haemorrhage. During the administration of anaesthesia, precautions as above are advised. The utmost care should be taken with vascular cannulation to prevent blood spillage. Contaminated sharps should be immediately disposed of in the correct receptacle. Needles should not be resheathed after venepuncture, since this increases the risk of needlestick injury. Care should be taken to minimise contamination with saliva and blood on tracheal intubation and extubation. Equipment should either be disposable or resterilised immediately after use. Induction and recovery in theatre, and the use of the minimum equipment compatible with safety, reduces the possible extent of contamination by the patient's blood. Contamination of the patient's clothing and skin with blood or drainage fluids should be reduced to a minimum before return to the ward.

In the case of needlestick injury, all guidelines recommend encouraging bleeding and liberal washing with soap and water. Blood testing for serology is only of use in providing a baseline should seroconversion occur as a result of infection.

Intensive care

The epidemiology of HTLV III suggests that the incidence of the disease in the community will continue to increase.[5,16] Current data suggest that about 19% or so of people with antibodies to the virus will develop the complete syndrome of AIDS. This leaves 80% of people who, while being potentially infective, are asymptomatic.[5] It is inevitable that there will be patients presenting to intensive care units with respiratory failure associated with AIDS. However, the larger problem relates to those patients who are HTLV III antibody positive but asymptomatic, who will present with a variety of conditions requiring intensive care management. This is not yet a major problem in this country, but will inevitably grow as the number of people exposed to the condition increases. It is of interest to consider whether these patients will respond to stressful conditions in the same manner as patients who have not been exposed to the virus, or whether they will demonstrate a degree of immunodeficiency even in the absence of florid symptoms.

Both groups of patients are potentially infectious and therefore present identical hazards in terms of intensive care management. The appropriate management of respiratory failure due to pneumocystis pneumonia in patients with AIDS is controversial in view of the apparently poor prognosis, and the role of intensive care has yet to be properly established. However, intensive care management is essential in a wide variety of conditions which can occur in patients who may be incidentally HTLV III antibody positive. In this regard there are obvious similarities to hepatitis B and many of the methods used to deal with that virus are appropriate for the management of patients with HTLV III.

General management. Most of the major aspects of management are described in the DHSS guidelines. Intensive care generally involves more hazards than in the general ward, due to the closer proximity of both medical and nursing personnel to the patient and to his excretions, secretions and blood. While the infectivity of secretions may be in doubt, it is obviously wise to treat them as potentially hazardous. The use of gloves is a sensible precaution and, if the patient has a productive cough, a mask may prevent droplet infection, although there are no positive or negative data regarding the infectivity of droplets in this condition. The use of goggles if there is a possibility of blood being spread about and gowns to minimise contamination of clothing if there is to be significant contact are both sensible precautions. Obviously, adequate methods of disposal of used equipment and dressings must be available.

It seems sensible to minimise the number of skin punctures performed, and in this regard it may be considered useful to place an arterial line if only to facilitate blood sampling. Similarly, central venous access may reduce the number of peripheral venous catheters required during an intensive care stay.

Staffing. The syndrome is relatively new and both medical and paramedical staff have been exposed to a considerable volume of information from both scientific and nonscientific sources. Consequently, there is considerable apprehension, anxiety and suspicion surrounding the admission of patients with HTLV III antibodies. Probably the most important aspect of the subsequent management of these patients in the intensive care unit is the adequate and rational education of the staff involved. Whilst the potentially disastrous consequences of infection should be explained, the apparently low infectivity of the virus should be stressed.[8,10,13] The actual mode of spread and infectivity of the virus may be somewhat similar to that of hepatitis B, and in this regard it should be noted that the incidence of hepatitis B infection in the medical community may be three times that of the normal community.[17] It has also been suggested that as some of the patients with this syndrome have a high incidence of cytomegalovirus infection, personnel who are pregnant should probably avoid close contact with the patients.[18]

Equipment. A great deal of the equipment used in the intensive care unit is available in disposable form and this simplifies management. However, capital items such as ventilators will need to be serviceable for other patients. Two approaches are possible. The first is to dedicate a ventilator for use with this particular group of patients, although this obviously means that if these patients rarely present in the intensive care unit, an expensive item of equipment is not available for general use. The second approach is to consider that the organism is susceptible to a variety of agents, and therefore that equipment may be relatively easily sterilised after use. For example, the Siemens Servo 900C may be used for these patients; disposable circuitry is used with bacterial filters on both inspiratory and expiratory limbs, to reduce the potential hazard of droplet infection. The inspiratory limb within the machine, the flow transducer and the expiratory limb may all be washed thoroughly in ethyl alcohol for one hour, rinsed in distilled water and then autoclaved in steam at 130–150°C for 15 minutes. Both chemical and heat treatment inactivate and destroy the virus.[18,19] The machine itself can then be wiped down with a variety of cleaning agents and is then able to be used on another patient.

This system of sterilising the ventilator is simple and easy to do and allows the use of a sophisticated ventilator in patients who may have complex respiratory problems. It does not necessitate the consequent dedication of this very expensive capital item of equipment for use only with that type of patient. This may be very important if the number of HTLV III antibody positive patients increases dramatically in the next couple of years.

The use of a blood gas analyser in intensive care is often a necessary part of management. A Corning 178 machine may be sterilised in the following way. The effluent container for the analyser should have 100 ml or so of 1% sodium hypochlorite solution added to it. The blood gas sample from the patient may be introduced into the machine in the normal manner, but with as little spillage as possible. Following analysis, up to 5 ml of sodium hypochlorite 1% are introduced into the machine and left for 5 minutes. The machine is then put through its wash cycle twice and a test calibration will then need to be done. It can then be used for the next patient sample.

Other testing is done in the laboratory and some of the techniques involved, especially with the larger analysers, involve the production of aerosols. This may be hazardous and in most departments it is preferred that these tests be done as individual runs following on from normal samples. A good liaison with the investigative department will enable most tests to be done, although it may be necessary to tailor the time of testing to fit in with the requirements of that department. Obviously, all samples should be well marked and designated as potentially infective for the safety of the people involved in their analysis.

Conclusion

The risk of transmission of AIDS from patient to health care worker appears to be low but, in view of the so far poor prognosis of the disease, precautions against spread must be taken. By maintaining a high index of suspicion, screening those patients at risk of carrying the virus and adhering to recommended precautions, risk to caring personnel may be minimised. Management similar to that of a patient carrying hepatitis B is adequate.

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Note

The recommendations stated above are the authors' current practice; as this is a rapidly changing field, further comment on the subject is welcomed.

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CASE REPORT

Ketamine by continuous infusion in status asthmaticus

P. J. STRUBE AND P. L. HALLAM

Summary

A 13-year-old girl was admitted to the intensive care unit with status asthmaticus. Conventional bronchodilator therapy failed to relieve her bronchospasm. In order to try and avoid artificial ventilation, a continuous intravenous infusion of ketamine was used with success. The total dose rate was 40 μg/kg minute for a period of 8 hours; this was given at a decreasing rate. She regained consciousness 30 minutes after the end of the infusion and became well orientated after one hour. Ketamine is a useful drug in the intensive treatment of status asthmaticus and should be tried before a decision is taken to start mechanical ventilation.

Key words

Anaesthetics, intravenous; ketamine.
Complications; asthma.

We report here a patient in whom conventional bronchodilator therapy failed to relieve bronchospasm, which was eventually controlled with an infusion of ketamine.

Case history

The patient was a 13-year-old, 35 kg girl who had been treated for severe chronic asthma since the age of 2 years. She also showed marked behavioural problems at home (including refusal to go to school) and on the ward, where she manipulated her mother. However, there was no doubt that her asthma flared up from time to time and, while usually well controlled on nebulised salbutamol at home, she had required frequent hospital admissions at a rate of one per month during the last year.

The present admission began with a 4-day history of upper respiratory tract infection and severe wheezing. On the ward she was treated with steam, high dose steroids and aminophylline by infusion, but deteriorated clinically with a worsening respiratory pattern; she became more distressed. She would not allow an arterial blood gas specimen to be taken, and would not let go of her mother. Her anxiety and distress were clearly aggravating her respiratory pattern and the need for sedation had to be carefully weighed against the risks of further respiratory depression. The intensive care unit received a request to admit, sedate, monitor her and finally to ventilate her lungs when necessary.

On admission to the unit she had a tachycardia (140 beats/minute). Her blood pressure was 110/60 mmHg. She was breathing rapidly, (30 breaths/minute) sitting up, using her accessory muscles, and holding onto her mother. There was marked intercostal recession, but chest expansion was fair and equal with loud ex-

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piratory wheezes in all areas. She was not cyanosed, dehydrated or pyrexial. She was alert, orientated and attention seeking, hoarsely crying to her mother not to leave her and pushing the nurses away. She continually removed her humidified oxygen mask and pulled on her intravenous infusion. Her mother said that neither of them had slept at all for 36 hours.

The situation demanded sedation or sleep for the patient and peace for the mother and father. Initially midazolam 20 mg was given slowly by increments and failed to produce lasting sedation, but did allow an arterial blood gas to be taken. This showed pH 7.29, $P\text{ao}_2$ 10.2 kPa ($F\text{io}_2$ 0.3) $P\text{aco}_2$ 6.2 kPa, BE −2 mmol/litre and saturation 97%.

One hour later she was wide awake, but disorientated and struggling noisily. Her respiratory rate had risen to 46 breaths/minute and the work of breathing looked considerable clinically. Before deciding to undertake artificial ventilation of her lungs, a trial of ketamine was considered. An initial dose of 50 mg intravenously was followed by continuous infusion of 90 mg/hour, for 8 hours, a rate equivalent to 40 μg/kg/minute. She became quiet but rousable and slept for long periods. Her respiratory pattern appeared more comfortable and the rate slowed to 30/minute. On auscultation her wheezing was less marked and her blood gases improved: pH 7.38, $P\text{ao}_2$ 11.3 kPa ($F\text{io}_2$ 0.3), $P\text{aco}_2$ 4.5 kPa, BE 0.5 mmol/litre. Her pulse and blood pressure remained unchanged. She continued on intravenous bronchodilators, steroids and ketamine, with nebulised salbutamol until the next day, when ketamine was decreased and gradually stopped. During 8 hours she had received 770 mg of ketamine. She woke up slowly, and after half an hour was fully conscious and alert, yet calm and cooperative. There was no psychic reaction and she remembered no dreams. The asthma was clearly improved enough for her to be discharged to the ward that morning. Later in the day she was able to eat, drink and get out of bed.

Discussion

Many regard ketamine as a useful tool to be reserved for the exceptional patient. Others have advocated ketamine, and especially its (+) isomer, as possessing most of the properties of the ideal intravenous anaesthetic agent.[1] Low dose continuous infusions have been used for postoperative analgesia, but it is not a sedative drug that is often used in intensive care. Interesting case reports regarding its successful use in treating severe bronchospasm which has proved refractory to conventional bronchodilators have appeared in the anaesthetic literature.[2-4] It has also been found to be effective in treating bronchospasm during halothane anaesthesia.[4] Because of its beneficial effect on airways resistance, ketamine has been advocated as the agent of choice for rapid induction of anaesthesia in patients with reactive airways disease.[1]

In early clinical studies, ketamine was noted to cause a decrease in airways resistance and an increase in pulmonary compliance in patients with reactive airways disease.[5,6] The respiratory response to CO_2 is maintained during ketamine anaesthesia,[7] and significant respiratory depression does not occur unless a rapid bolus injection is given. Slow injection of 2 mg/kg over 60 seconds produces a nonsignificant change in arterial $P\text{ao}_2$ or arteriovenous oxygen tension difference.[8] Improved oxygenation and decreased shunting has been reported during one lung anaesthesia;[9] the difference is due to ketamine preserving the hypoxic vasoconstriction reflex.

The ability of ketamine to antagonise antigen-induced bronchospasm may be related to its vagolytic and direct smooth muscle relaxant effects. However, the major effect *in vivo* appears to be secondary to sympathomimetic properties caused primarily by direct central nervous system stimulation. The bronchodilator effects are prevented by β-adrenoceptor blockade. There is little doubt that ketamine protects against asthmatic attacks during induction of anaesthesia in symptom-free asthmatic patients. Both halothane and ether can provide similar protection. Ketamine is also highly effective in producing bronchodilatation in patients with wheeze present at the time of induction. In patients with status asthmaticus, wheezing has returned under halothane anaesthesia after initially clearing during induction with ketamine. Wheezing diminished after additional intravenous ketamine. Reappearance of asthma each time the depth of anaesthesia lightened, and clearing of the wheezing with the deepening of the dissociative state, has been observed by Betts and Parkin.[2] Reporting on the management of status asthmaticus some authors still recommend the use of ether for patients whose lungs are being ventilated.[10] However, ketamine has fewer disadvantages and would appear to be the drug of choice today for the sedation of ventilated asthmatics.

The use of a continuous infusion of ketamine for status asthmaticus on intensive care has been reported before, but in a patient whose lungs were already being ventilated.[4] On this occasion, unnecessary intubation and ventilation were avoided, along with the attendant risks of barotrauma. An infusion of 10–30 μg/kg/minute has been shown to minimise the unwanted cardiovascular and central nervous side effects of ketamine.[1] These are both further attenuated by the addition of midazolam. Infusions of 48 hours duration have been followed by rapid awakening.[4]

More is now known about the metabolism of ketamine. It is broken down by hepatic microsomal enzymes to norketamine, which itself has some anaesthetic activity. The elimination phase of the drug has a half life of 100–180 minutes, similar to that of midazolam (mean 120 minutes), shorter than methohexitone (97–240minutes) and much shorter than diazepam (20–50 hours). Using a continuous infusion of ketamine, Idvall *et al.*[11] reported an elimination $t_{1/2}$ of 79 minutes. However, like all these drugs ketamine has potential for accumulation and the infusion rate should be progressively reduced.

As etomidate is no longer recommended for use by continuous infusion in the intensive care unit, and as Althesin has been withdrawn, there is a need for a drug that can be given by continuous infusion to sedate such patients. Ketamine deserves to be reconsidered for this purpose. It has many desirable features. The main disadvantage is hallucinations, which can be minimised, and accumulation which is not marked in practice.[12] Used cautiously, ketamine can be a valuable additional drug in the treatment of acute asthmatic patients on intensive care.

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CASE REPORT

Cervical epidural anaesthesia in carotid artery surgery

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Summary

The successful anaesthetic management using a cervical epidural technique is reported in three patients undergoing carotid artery surgery. Adequate analgesia was obtained in all cases and the adequacy of cerebral blood flow was easily judged by the patient's state of consciousness. Cervical epidural anaesthesia could be a safe and reasonable technique for the management of patients who need carotid artery surgery.

Key words

Anaesthetic techniques; cervical epidural.
Surgery; carotid artery.

Anaesthesia for carotid artery surgery has been performed using a variety of techniques, including intravenous and inhalational general as well as regional methods; each has its advantages and disadvantages. There has been some controversy concerning the appropriate anaesthetic management of patients who need temporary carotid artery occlusion during surgery. Many of these patients are elderly and hypertensive, and have generalised arterial atherosclerosis including the cerebrovascular system. Therefore, cerebral ischaemia may occur during carotid artery clamping, even with the use of a temporary bypass shunt.

General anaesthesia has usually been advocated because of certain incidental advantages, including the ability to control the patient's ventilation and the avoidance of the potential hazards of airway obstruction and agitation in an uncooperative patient.[1] However, with regional anaesthesia, it is possible to observe the patient's level of consciousness and neurological state on cross-clamping of the carotid artery.[2,3] This report presents the anaesthetic management of three patients undergoing carotid artery surgery using cervical epidural anaesthesia.

Case histories

Case 1

A 61-year-old woman who weighed 31 kg was admitted for evaluation of a pulsatile mass in her neck, which had gradually enlarged for a year. Carotid angiography revealed a left carotid arterial aneurysm between the common and the internal carotid artery.

She was scheduled for resection of the aneurysm and vascular reconstruction. At preoperative rounds, we explained the epidural anaesthetic plan including the intra-operative awake condition. Premedication consisted of

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0.5 mg atropine and 50 mg hyroxyzine, administered intramuscularly.

In the operating room, an epidural catheter was inserted into the C_{6-7} interspace and advanced 5 cm cephalad with the patient in the left lateral decubitus position; 15 ml lignocaine 0.8% was administered through this. The onset of analgesia between C_2 and T_1 was confirmed by a skin pinprick test, surgery was then started and 4 litres/minute of oxygen was administered through a nasal cannula. Two hours later, the patient's consciousness was lost following complete clamping of the left carotid artery and clamping was immediately released. Within 10 seconds of declamping, she recovered consciousness. The vascular reconstruction of the left common–internal carotid artery with a vein graft was carried out with the aid of a temporary bypass. Adequate analgesia was obtained during the surgery. Postoperatively, the patient was fully conscious; however, right hemiparesis and a right Babinski sign were present.

Case 2

A 59-year-old man who weighed 54 kg was admitted for evaluation of a bruit in the neck. Past history was unremarkable except for hypertension which was well controlled by oral diuretics. Angiography revealed significant narrowing of the left internal carotid artery and he was scheduled to undergo left carotid thrombo-endarterectomy. Pre-operative explanation and premedication were similar to the first case.

In the operating room, the cervical epidural catheter was inserted into the C_{6-7} interspace and placed 5 cm cephalad. The trachea was intubated (following 250 mg of thiamylal and 60 mg of intravenous suxamethonium) lest respiratory depression were caused by the epidural infusion of local anaesthetic. Intermittent epidural infusion of 2% lignocaine, 2–3 ml at a time, was carried out and a total of 29 ml was administered. The patient breathed spontaneously 67% nitrous oxide in oxygen. Administration of nitrous oxide was stopped prior to carotid artery clamping. Blood gas analysis showed $P\text{aO}_2$ 53.3 kPa, $P\text{aCO}_2$ 5.3 kPa with 100% oxygen. When the left common carotid artery was clamped, the level of consciousness remained unchanged. Endarterectomy was performed using a temporary bypass between the internal and the common carotid artery. Postoperatively there were no abnormal neurological signs.

Case 3

A 67-year-old man who weighed 62 kg who had suffered from transient ischaemic attacks for 3 years, was admitted for intermittent claudication. After iliac surgery a left carotid thrombo-endarterectomy was planned for the narrowing of the left internal carotid artery which was revealed by angiography. Pre-operative management was as described for case 1.

The epidural catheter was inserted into C_7–T_1 interspace and placed 5 cm cephalad. The trachea was intubated as before. Following the epidural infusion of 13 ml of 2% lignocaine, anaesthesia was maintained with 67% nitrous oxide in oxygen. Blood gas analysis showed $P\text{aO}_2$ 51.6 kPa and $P\text{aCO}_2$ 5.1 kPa with spontaneous respiration. As before, nitrous oxide administration ceased prior to carotid artery clamping. Just after clamping of the left internal and external carotid artery, the patient's responses to our requests (opening eyes, and gripping or foot lifting) entirely disappeared, although such responses had been present prior to clamping. Immediately, the clamp was removed and surgery was discontinued because it was impossible to maintain consciousness during construction of a temporary bypass. The patient fully recovered consciousness in approximately 20 minutes. This syncope attack may have been due to the insufficient circulation of the left anterior cerebral artery which had been shown during pre-operative angiography.

Discussion

Although a debate continues between advocates of general and regional anaesthesia for carotid artery surgery, general anaesthesia is frequently chosen because of the improved ability to manipulate regional cerebral blood flow by changes in $P\text{aCO}_2$ and systemic blood pressure.[1] On the other hand, regional anaesthesia offers a definite advantage in allowing evaluation of the patient's neurological status.

Connolly and associates[4] reported a series of 102 endarterectomies performed with the patients awake under cervical plexus block. They stated that few patients were unable to tolerate the operation under local anaesthesia.

Takasaki and associates[5] reported that cervical epidural anaesthesia with 2% mepivacaine reduced mean inspiratory capacity and vital capacity by 25%. We used 0.8% lignocaine in case 1 and no respiratory depression was noted. However, due to the uncertainty about the analgesia, we used 2% lignocaine thereafter. The trachea was prophylactically intubated for fear of hypoventilation caused by cervical epidural infusion of 2% lignocaine in the second and third cases. Tracheal intubation was well tolerated in both patients with inhalation of 67% nitrous oxide in oxygen.

There have been many reports concerning monitoring of the adequacy of cerebral blood flow during carotid artery surgery. Moore and associates[6] stressed the clinical importance of internal carotid artery back pressure (the stump pressure). They reported that the minimum safety value was 3.3 kPa. However, the study by Sublett and associates[7] did not entirely confirm that value. Monitoring of the jugular venous oxygen saturation during carotid occlusion was undertaken by Larson *et al.*[8] However, they concluded that it was a poor indicator of loss of consciousness or development of neurological deficits. Harris and associates[9] had a better experience with the EEG (electroencephalogram) as a monitor in 88 patients under cervical plexus anaesthesia, and reported a good correlation between changes in the EEG and the cerebral blood flow. However, a neurologist is usually required to be present in order to interpret the recordings accurately.[9] Boysen and associates measured cerebral blood flow by xenon-133 clearance during carotid endarterectomy and found that neurological deficits develop when it is reduced to 20–30 ml/100 g/minute.[10] However, this technique is difficult to perform in clinical circumstances.

Therefore, although a number of techniques have been described, they are either not very reliable or are clinically unavailable. When regional anaesthesia is employed, the patient's state of consciousness can be observed closely, and loss of consciousness, which is a good indicator of reduced cerebral blood flow, can be easily and promptly recognised.

We performed cervical epidural anaesthesia in place of cervical plexus block, which has been previously reported.[4,9] We consider that cervical epidural anaesthesia may be superior to cervical plexus block for a number of reasons: a supplemental dose can be given easily, without interfering with surgery (even if the surgery is prolonged); cervical epidural anaesthesia may provide better anaesthesia and more comfortable peri-operative conditions than cervical plexus block; peri-operative hypertension, which occurs frequently in patients who undergo carotid endarterectomy, may be less marked because of inhibition of peripheral sympathetic vascular tone; the epidural catheter can be employed for post-operative analgesia.

Finally, we must admit that cervical epidural anaesthesia is not without the potential for complications. However, Wittich and associates have reported on over 200 patients using epidural anaesthesia for head and neck surgery, and affirmed its safety.[3] In addition, we have inserted cervical epidural catheters in more than 100 cases for over 10 years, (for the purposes of relief of severe pain due to cervical bone metastases, cervical spondylosis, rheumatoid arthritis, etc). During this period, we have never experienced any severe complications such as laceration of the spinal cord, significant hypotension, respiratory arrest or haematomata. However, in our opinion, this technique must be carried out by a skilled anaesthetist using sufficient cardiopulmonary monitoring.

In conclusion, we suggest that regional anaesthesia, particularly cervical epidural anaesthesia, is a safe and reasonable technique for the management of patients who require carotid artery surgery.

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Anaesthesia, 1986, Volume 41, pages 1024–1025

CASE REPORT

Delayed convulsions following enflurane anaesthesia

I. S. GRANT

Summary

A case of convulsions which occurred 3 days after recovery from enflurane anaesthesia is reported.

Key words

Anaesthetics, volatile; enflurane.
Complications; convulsions.

The possible association of convulsive electroencephalographic (EEG) activity with enflurane anaesthesia is well recognised. Several recent reports have described convulsions in non-epileptic subjects during recovery from enflurane anaesthesia.[1-3] While EEG changes may persist for many days after exposure,[4,5] reports of convulsions occurring later than 3 days after recovery from enflurane are rare.[6]

Case history

A previously healthy 24-year-old man with no personal or family history of epilepsy presented for surgery for osteochondritis of the knee. He had previously undergone surgery to his knee on five occasions over a 15-month period prior to the present surgery. Enflurane had been employed on all occasions, in view of the possible hepatic consequences of repeated halothane exposure. Anaesthesia on each occasion was induced by thiopentone, maintained with nitrous oxide and enflurane in oxygen, and was essentially unremarkable. However, nursing staff reported that the patient was always extremely slow to recover fully and was drowsy for 2 or 3 days postoperatively.

He was admitted on the morning of operation and was not premedicated. Anaesthesia was induced by methohexitone 100 mg and maintained with nitrous oxide 66% and enflurane maximally 5% reducing to 1.5% in oxygen with spontaneous ventilation via a Bain system. Morphine 5 mg was administered intravenously for analgesia.

Immediate postoperative recovery was rapid; the patient returned to the ward fully conscious about 30 minutes after the end of surgery. Thereafter, periods of drowsiness similar to the previous occasions occurred over the next 48 hours. Three days after surgery he was discharged home and about 10 hours after discharge he had a grand mal convulsion. Emergency treatment with intravenous diazepam 10 mg led to cessation of the fit after 15 minutes and the patient was admitted to an acute medical ward. He was twitchy, hypertonic and hyperreflexic for several days and had further apparent fits, without fully losing consciousness, 7 days and 9 days postoperatively.

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Neurologically, apart from a left VI nerve palsy which resolved within a few days, there were no focal signs. Computerised axial tomography revealed no abnormality, but an EEG 4 days postoperatively revealed a single episode of rhythmic sharp activity anteriorly on the right side. Repeat EEG examination 8 days later was normal. The patient made a full recovery and was discharged home again 12 days postoperatively on no medication.

Discussion

Enflurane anaesthesia is associated with high amplitude spikes and periods of electrical silence on the EEG.[7] The hyperexcitability appears to originate in the limbic system, with subsequent spread to all other areas.[8] It is potentiated by increasing concentrations of enflurane and by hypocapnia. Small doses of thiopentone, methohexitone or diazepam may potentiate the seizure activity by selectively impeding ascending inhibitory pathways from the brain stem reticular formation.[8]

In cats, there is a prolonged period of abnormal EEG activity of up to 16 days following enflurane anaesthesia, although initially normal from 2–24 hours after exposure.[7] In human subjects, two cases of delayed convulsions have occurred 6 and 8 days postoperatively after enflurane anaesthesia,[6] while EEG abnormalities have persisted 2 days postoperatively in a patient who had a single grand mal convulsion one hour after recovery from enflurane anaesthesia.[4] Delayed seizure activity, whether clinically apparent or on EEG, has not been fully explained, but it has been attributed to the presence of fluorinated metabolites which are excreted in the urine for 17 days after exposure to enflurane.[9]

It is tempting to speculate that this patient's previous postanaesthetic drowsiness may have been attributable to subclinical convulsions and that the final overt convulsion may have been provoked by enzyme-induced accumulation of metabolites due to the frequent re-exposure to enflurane. However, investigation of prior administration of enzyme-inducing drugs to patients undergoing anaesthesia has failed to demonstrate an increase in enflurane defluorination,[10] while studies of repeat enflurane administration to volunteers have detected no increase in urinary fluoride excretion.[11]

The problem of delayed convulsive activity following enflurane anaesthesia clearly requires further elucidation.

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Anaesthesia, 1986, Volume 41, pages 1026–1028

CASE REPORT

Anaesthesia and the subclavian steal syndrome

R. J. THOMPSON

Summary

Anaesthesia in two patients with subclavian steal syndrome is described. Both patients showed an interesting response to hyperventilation. The mechanism of this response and its implications for the anaesthetist are discussed.

Key words

Arteries; subclavian artery.
Complications; subclavian steal syndrome.

The subclavian steal syndrome occurs when there is a block in a subclavian artery between its origin at the aorta and the origin of the ipsilateral vertebral artery (Fig. 1). If the affected arm is exercised, the increased blood flow required is provided by retrograde flow in the ipsilateral vertebral artery and is thus 'stolen' from the circle of Willis. Cerebral blood flow is decreased and the patient may complain of dizziness or may lose consciousness.

Case histories

Case 1

The patient was a 53-year-old female with a right-sided systemic arterial blood pressure of 130/80 mmHg and a pulseless left arm who complained of the classical symptom of dizziness when carrying a shopping bag in her left hand. She was scheduled to undergo an arch aortogram under general anaesthesia.

Premedication consisted of diazepam 10 mg and atropine 0.6 mg. Induction of anaesthesia and tracheal intubation with a cuffed tube were carried out with thiopentone 250 mg and suxamethonium 50 mg; anaesthesia was maintained with nitrous oxide 6 litres/minute plus 3 litres/minute and trichloroethylene.* Alcuronium was used to provide muscle relaxation. Arterial blood pressure was monitored by oscillometry.

After commencement of anaesthesia, the left radial artery was palpated (force of habit) and found to be present. The blood pressure cuff was transferred to the left arm and subsequently from arm to arm so that the blood pressure chart (Fig. 2) could be constructed. A review of the anaesthetic technique and of the pathophysiology of the syndrome suggested that hyperventilation

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*Trichloroethylene was vaporised via a chloroform bottle. 'Minimal' in the text means that the lever was in the horizontal position, 'increased' means that the lever was almost vertical.

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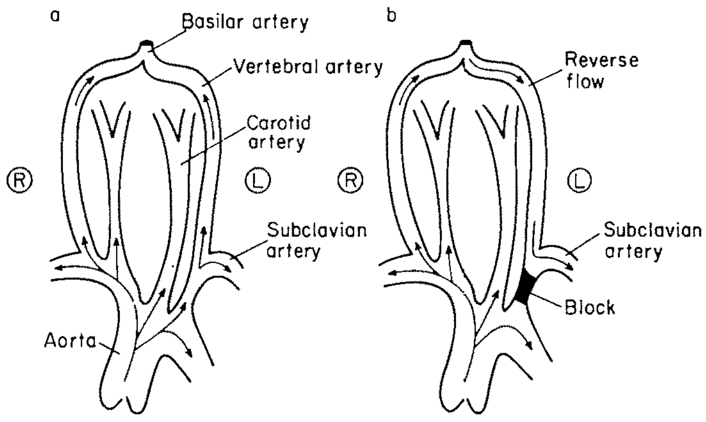

Fig. 1. (a) Normal anatomy; (b) left-sided block at origin of subclavian artery. An increase in reverse blood flow in the vertebral artery may lead to a critical reduction in cerebral blood flow due to a 'steal' phenomenon.

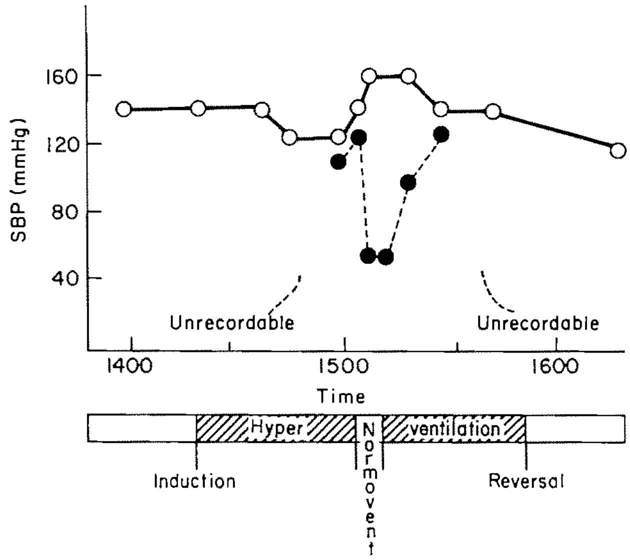

Fig. 2. Arterial blood pressure in the left and right arms of case 1 during anaesthesia. During hyperventilation the arterial blood pressure in the left arm approached that in the right arm. ○—○, Right SBP; ●---●, left SBP.

might be an important factor in producing this change; ventilation was therefore decreased to 6 litres/minute for 8 minutes, trichloroethylene concentration was increased and 4% CO_2 was added for the first minute. This caused a large fall in the left arm blood pressure, as can be seen from Fig. 2. On return to 9 litres/minute gas flow, left-sided pressure again approached that in the right arm. Throughout the procedure the pulse in the left arm lagged behind that in the right.

Postoperative progress was uneventful. On visiting the patient on the second postoperative day, she was asked to hyperventilate; after 20 seconds she became extremely dizzy and a good pulse appeared in the left arm, with a systolic blood pressure of 80 mmHg. At this point she

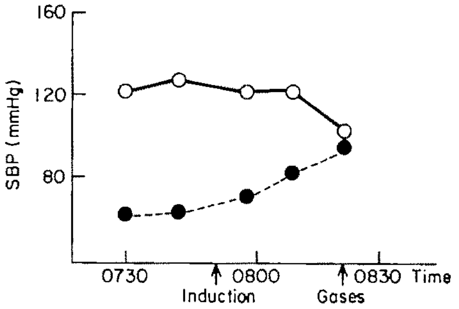

Fig. 3. Hyperventilation after induction of anaesthesia in case 2 resulted in an increase in the arterial pressure in the left arm. Blood for blood gas analysis was taken as indicated. ○—○, Right SBP; ●---●, left SBP.

seemed in imminent danger of fainting and the experiment was stopped.

The arch aortogram showed a block of the left subclavian artery proximal to the vertebral artery and this condition was later corrected in another hospital.

Case 2

This patient had an arterial blood pressure of 130/80 mmHg in her right arm and a systolic pressure of 40 mmHg in her left arm. She was scheduled to undergo surgical excision and grafting of a known left subclavian block, proximal to the origin of the left vertebral artery.

Premedication consisted of papaveretum 10 mg and atropine 0.6 mg. Anaesthesia was induced with thiopentone and suxamethonium administered to facilitate passage of a cuffed tracheal tube. Maintenance of anaesthesia was with nitrous oxide 6 litres/minute plus oxygen 3 litres/minute, supplemented by incremental pethidine; manual ventilated was provided via a circle absorber.†

The surgical team were prepared to allow arterial blood sampling to be undertaken in the anaesthetic room from the right arm while manipulation of the $Pa\text{CO}_2$ was performed. It was thought unwise to cannulate the left subclavian artery. The results are shown in Fig. 3. At the time of blood gas sampling, the systolic blood pressure on the right had fallen to 90 mmHg while that on the left had risen to 85 mmHg; the left-sided pulse lagged behind the right as it had done pre-operatively. Blood gas values were $Pa\text{O}_2$ 21 kPa; $Pa\text{CO}_2$ 2.9 kPa; pH 7.55; HCO_3 19.5 mmol/litre; O_2 saturation 99.5%.

Discussion

It would seem that in both these patients there was a correlation between hyperventilation and flow in the left subclavian artery, and the changes which occur during hyperventilation may explain this. The author's hypothesis is that as $Pa\text{CO}_2$ falls, the vasoconstriction which occurs distal to the circle of Willis would provide an increased pressure head of blood which would readily flow in a retrograde direction down the vertebral artery; this would produce an increased pressure in the affected arm, as demonstrated in these two patients. That the pulse on the affected side lagged that on the contralateral side suggests that the pathway of flow was as outlined above, rather than that anaesthesia had in some way altered the nature of the block.

It would therefore seem unwise to hyperventilate these patients, in view of the potential for stealing blood from the circle of Willis. The rapidity of onset of dizziness in the first patient, when hyperventilating voluntarily, suggests that this could be a significant problem. Any patient with an absent pulse in one arm should be viewed with suspicion and if pre-operative hyperventilation produces a palpable pulse in the affected limb the presence of a subclavian steal syndrome should be suspected. Indeed, this simple test might well provide a useful adjunct in the diagnosis of the syndrome.

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†The technique used for intermittent positive pressure ventilation in this particular hospital was intermittent pethidine in total doses which commonly ranged from 200–400 mg and a fresh gas flow rate of 9 litres/minute, delivered via a circle system with the absorber removed. The absorber was used in this case to provide hypocapnia.

Anaesthesia, 1986, Volume 41, pages 1029–1031

CASE REPORT

Severe upper airway obstruction and difficult intubation in cicatricial pemphigoid

B. DRENGER, M. ZIDENBAUM, E. REIFEN AND E. LEITERSDORF

Summary

Upper airway obstruction in cicatricial pemphigoid is rarely seen by the anaesthetist. A case of severe dyspnoea due to progressive laryngeal obstruction is presented. Tracheal intubation during induction of general anaesthesia for permanent tracheostomy was extremely difficult and was successfully performed by introducing a size 12 French suction catheter through the stenotic laryngeal orifice. Adequate ventilation was achieved by using the oxygen flush valve to deliver oxygen intermittently through the catheter.

Key words

Airway; obstruction.

A case is described in whom there was exceptionally severe laryngeal involvement in cicatricial pemphigoid. Distortion and stenosis of the vocal cords caused severe respiratory distress and rendered tracheal intubation almost impossible.

Cicatricial pemphigoid is a rare variant of bullous pemphigoid, which primarily affects the mucosal surfaces, but in 25% of patients cutaneous lesions also occur. The vesicular eruption heals by retraction and becomes secondarily scarred and thickened. In those cases with involvement of the trachea and larynx, the upper airway may be gradually occluded with the production of stridor, dyspnoea and cyanosis.

Case history

A 27-year-old woman was referred from another hospital to the Department of Dermatology of the Hadassah University Hospital due to progressive dyspnoea, stridor and intermittent attacks of laryngospasm during the previous month. Oral involvement of the disease had been noticed for the last 2 years, manifested clinically as painful mouth erosions developing into cicatrical lesions. There was also involvement of the nostrils, lips, gingiva, tongue and posterior palate. Indirect laryngoscopy showed that the larynx and epiglottis were extensively affected and distorted by adhesions. The laryngeal orifice was narrowed to 4 mm with minimal movement of the vocal cords. The mucosa was oedematous, friable and bled easily. Biopsy, which was taken from the oral mucosa, confirmed the diagnosis of benign mucous pemphigoid. The conjunctivae were severely affected and almost complete loss of vision ensued.

Conservative treatment was instituted with humidified oxygen, high dose intravenous dexamethasone, atropine and adrenaline and oral azathioprine. There was an initial response to treatment, but subsequently the patient con-

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tinued to deteriorate with reappearance of severe dyspnoea and cyanosis. Due to the increasing respiratory distress and the unremitting nature of the disease, a permanent tracheostomy was suggested as a life saving procedure. Because of the anxiety of the patient and her inability to co-operate, general anaesthesia was chosen. Also, any stimulus in the nasopharyngeal area produced severe emotional stress, tachypnoea, aggravated the cyanosis and even led to an attack of laryngospasm.

Tracheal tubes size 4 and 5 mm, and a rigid bronchoscope (No. 4) were prepared. The patient was anaesthetised, while she was breathing spontaneously through a facemask, with intravenous thiopentone (3 mg/kg) and the inhalation of increasing concentrations of halothane (up to 2%) in oxygen. No muscle relaxants were given and laryngoscopy was performed when the jaw muscles were relaxed by the halothane. At that time, the extensive involvement of the disease was clearly seen. The mucosa was friable and bled on contact. The epiglottis was distorted and rigid, and it was difficult to see the vocal cords. A small opening, assessed as 3–4 mm, was observed in the anterior part of the laryngeal orifice, with partial movement of the cords. Attempts at tracheal intubation with a 4 mm tracheal tube and a rigid No. 4 bronchoscope were unsuccessful. 'High flow' oxygen was continuously administered directly above the vocal cords and the surgeon was ready to perform emergency cricothyrotomy. However, in a repeated trial of tracheal intubation, a size 12 French suction catheter was successfully introduced. Good expansion of the lungs was obtained with high flows of oxygen. As the leakage of expired air around the suction tube was minimal, the oxygen source was disconnected every few breaths in order to avoid overdistention of the lungs. Anaesthesia was maintained with 10 mg of diazepam and 0.1 mg of fentanyl and, using local anaesthesia with 1% lignocaine, an unhurried formal permanent tracheostomy was performed. During the entire procedure the patient appeared to be adequately oxygenated and anaesthetised.

Throughout the postoperative period, a continuing improvement in the general condition was noted and no further respiratory obstruction occurred.

Discussion

Involvement of the oral and nasal mucosa are frequently encountered in pemphigus and in bullous pemphigoid, but it usually occurs with sparing of the larynx itself. In cicatricial pemphigoid, lesions of the larynx and oesophagus are common,[2] but the combined treatment of high dose steroids and chemotherapy usually limit the severity of the disease.[3] Severe obstruction of the upper airway in the cicatricial variant of the disease is rarely seen by the anaesthetist and tracheostomy is needed only in advanced cases. Upper airway obstruction in these patients is usually due to obstruction at the level of the vocal cords and is complicated by severe ulceration, adhesions and deformities of the oropharyngeal mucosa, epiglottis and web adhesions of the vocal cords.[1]

Upper airway obstruction becomes clinically apparent when the diameter of the laryngeal orifice is narrowed to 3–4 mm.[1] Stridor and dyspnoea are the main symptoms. The obstruction is further aggravated during inspiration, as the walls of the glottis are drawn together by the negative intratracheal pressure.

Probably the most appropriate anaesthetic for tracheostomy in these cases is local anaesthesia, while the patient is breathing a mixture of 20% oxygen and 80% helium. As flow of air in large airways is turbulent and density-dependent, breathing a mixture of low density gas through an upper airway obstruction produces less turbulence and increases the flow by 70% relative to air.[1] The use of less dense gas in upper airway stenosis will improve the maximal flow–volume ratio as shown by spirometry, as well as the driving pressure needed to overcome the rigid resistance of an orifice of 3 mm, as presented in the patient described here.

In the present case, the use of local anaesthesia was not feasible because of the patient's inability to cooperate and because of the unavailability of helium mixtures at that time.

Conclusion

This case confirms that anaesthesia of a patient with cicatricial pemphigoid and severe involvement of the oropharynx and larynx is extremely hazardous. Severe stridor is likely to be caused by a laryngeal orifice with a diameter of less than 3–4 mm and anaesthesia should be performed only after careful evaluation of the patient by indirect laryngoscopy and lung function tests.

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Anaesthesia, 1986, Volume 41, pages 1032–1035

APPARATUS

Dinamap arm and thigh arterial pressure measurement

S. L. GOLDTHORP, A. CAMERON AND A. J. ASBURY

Summary

Two automatic arterial pressure monitors (Model 1846 P) were used in 30 patients to measure arterial pressures and heart rates in the thigh and arm. Significant differences were found in thigh-arm sytolic ($p < 0.001$) and diastolic pressures ($p < 0.05$). Arm pressures could be predicted from leg pressures and correction factors are suggested. Mean pressures in the thigh approximated more closely to the calculated mean pressures than in the arm. These differences were of little clinical importance.

Key words

Measurement techniques; blood pressure.

The device for indirect noninvasive automatic mean arterial pressure measurement (Dinamap) is one of the few recently introduced monitors to gain wide acceptance in anaesthesia. The instrument is microprocessor-controlled so that the oscillometric method is applied meticulously according to a predetermined schedule. Dinamaps have a particularly useful feature whereby a reading is only considered true if it has resulted from two similar pulse waves. Individual pressure measurements are associated with a 95% confidence interval of ± 16 mmHg.[1] The Dinamap may be used for measurements over a wide range of limb sizes and suitable cuffs are available. The dimensions of these are in accordance with the latest recommendations of the American Heart Association (AHA).[2]

Measurements of arm and thigh pressures using recommended cuff sizes have long shown that thigh pressures are consistently greater, although closely correlated with arm pressures.[3] Although the pressure relationships between the different sites in the arterial tree are interrelated,[4] there is no statistical difference between invasive pressure measurements made in the femoral and brachial arteries in the supine position.[5]

The objectives of this study were to evaluate the relationships between arm and thigh pressures measured by two Dinamaps and to explore the relationships of the measured mean arterial pressure (MAP) to the systolic and diastolic arterial pressures (SAP and DAP). This information is important in situations where the anaesthetist is denied access to the arms due to the nature of the surgical field, fistulae, burns, plasters or amputations.

MAP is not a commonly used variable in noninvasive measurement and should ideally be

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derived from the integral of the arterial waveform. When necessary,[3] it has been calculated from the SAP and the DAP using the expression:

$$\text{MAP} = 0.33\ \text{SAP} + 0.66\ \text{DAP}$$

Former generations of the medical profession have used this equation to calculate MAP, but we have been unable to trace any paper where the formula has been derived. It remains in current usage and it was of interest to find whether the MAP measured by the Dinamap was the same as that commonly calculated from the SAP and the DAP.

Methods

Thirty unselected, physiologically stable patients aged between 23 and 76 years were studied during recovery from general anaesthesia. Arm and thigh pressure measurements were made simultaneously using two recently calibrated Dinamaps (Models 1846P). Cuff sizes were chosen according to the limits printed on the cuff fabric and were placed at the midpoints of the arm and thigh. The midpoint circumferences were measured with a standard tailor's tape. The Dinamap pressure hoses were then interchanged, allowing a 3-minute interval between pairs of recordings. The pulse rate, systolic, mean and diastolic arterial pressures were recorded on each occasion.

To check that the Dinamaps were performing in a similar way, the significance of the differences in pressure measurements and pulse rates in the 30 cases were determined using paired *t*-tests. Data derived from both machines were then combined, to give 60 measurements and the arm versus thigh measurements compared using paired *t*-tests. Linear regression was used to further explore the relationship.[6]

Linear regression was used to examine the relationship between the measured MAP and that calculated from the SAP and the DAP. Calculated means were derived using the equation above.[3] Multiple linear regression was used to assess the reasonableness of this equation in respect of the Dinamap's own measured mean. A probability value of $p<0.05$ was considered significant and $p < 0.01$ highly significant.

Results

Table 1 shows the results of the comparison between the two Dinamaps. Only in the case of systolic pressure measurements in the thigh was

Table 1. Measurement means (SEM) for each Dinamap.

	Arm pressures (mmHg)				Thigh pressures (mmHg)			
	Systolic	Diastolic	Mean	Arm pulse (beats/ minute)	Systolic	Diastolic	Mean	Thigh pulse (beats/ minute)
Dinamap 1	123.2	67.6	90	70.7	128	61	85.5	68.1
n = 30	(4.2)	(3.2)	(3.6)	(3.5)	(4.1)	(2.5)	(3)	(3.2)
Dinamap 2	121.6	67	88.2	69.1	137	64	88.2	70.2
n = 30	(4.7)	(3)	(4.1)	(3.2)	(4.7)**	(2.8)	(3.3)	(3.6)

**$p<0.01$.

Table 2. Arm versus thigh measurements on pooled data ($n = 60$)

		Pressure (mmHg)			
		SAP	DAP	MAP	Pulse (beats/ minute)
Paired *t*-test results	Arm mean	122.4	67.5	89.1	69.9
	(SEM)	3.1	2.2	2.7	2.4
	Thigh mean	132.9**	63.2*	86.4	69.1
	(SEM)	3.2	2.3	2.3	2.4
Linear regression results	Correlation coefficient – *r*	0.74**	0.62**	0.68**	0.98**

there a consistently significant difference. Table 2 shows the results of the comparison of means of the simultaneously measured arm and thigh pressures using the pooled data. These means are only statistically significantly different for the SAP and the DAP.

When linear regression (Table 2) was used to examine the relationship between the pressures and pulse rates, all produced statistically significant correlation coefficients. This suggests that it would be in order to make pressure predictions using the calculated regression equations. (Figs 1–3). Note, however, that the slopes of the best fit lines differ from one, and also that each equation has an intercept.

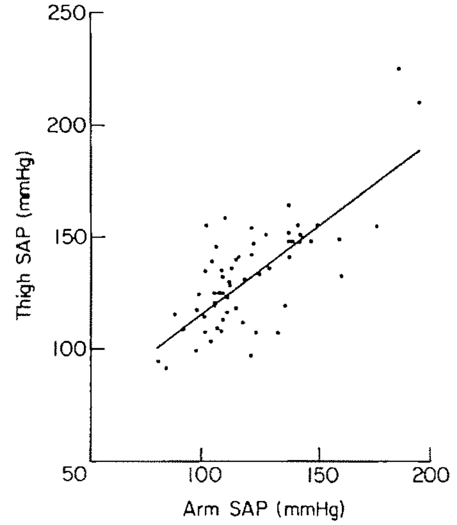

Fig. 1. Scattergram of arm versus thigh SAP results. The regression equation with standard errors is:
thigh SAP = 41 + 0.75 arm SAP
(mmHg) (11.08) (0.09) (mmHg)

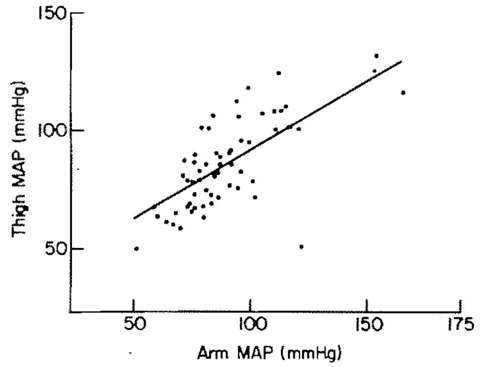

Fig. 2. Scattergram of arm versus thigh MAP results. The regression equations with standard errors is:
thigh MAP = 34 + 0.58 arm SAP
(mmHg) (7.45) (0.08) (mmHg)

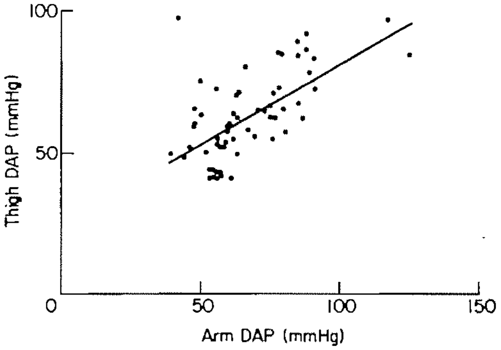

Fig. 3. Scattergram of arm versus thigh DAP results. The regression equation with standard errors is:
thigh DAP = 25 + 0.55 arm DAP
(mmHg) (6.47) (0.09) (mmHg)

Table 3 shows the relationship between the measured mean and the mean calculated from the standard formula.[3] There is a statistically significant difference between the measured mean and the calculated mean for the arm values ($p < 0.001$), but not for the thigh values. The correlation coefficients were 0.94 and 0.79 respectively, which were highly significant with respect to zero. The linear regression equations relating measured and calculated means are presented in Table 4. Note that the slope of the equation for

Table 3. Comparison measured and calculated MAPs ($n = 60$)

		Arm	Leg
Paired *t*-test results	Measured MAP	89.1	86.4
	(SEM)	2.7	2.3
	Calculated MAP	85.5**	86.0
	(SEM)	2.4	2.1
Linear regression results	Correlation coefficient – *r*	0.94**	0.79**

Table 4. Linear regression equations for experimental versus predicted arm and thigh mean (in the form $y = a + bx$, where y = measured mean, x = calculated mean with SE's)

Equation	Standard errors	
	a	*b*
y (arm) = $-1.78 + 1.06x$	4.4	0.5
y (thigh) = $17.78 + 0.8x$	8.25	0.09

the arm data has the lowest intercept and a slope nearest one.

Multiple linear regression to explore the relationship between measured MAP, SAP and DAP produces different equations for arm and leg pressures:

$$\text{MAP (arm)} = 0.506\ \text{SAP} + 0.495\ \text{DAP} - 6.323$$
$$\text{MAP (leg)} = 0.267\ \text{SAP} + 0.638\ \text{DAP} + 11.33$$

The coefficients of multiple regression were 0.94 and 0.84 respectively.

Discussion

The data from the two Dinamaps show statistically significant differences between the arterial pressures measured in the thigh and arm. These differences were greater for SAP than DAP, with no differences in the MAP or pulse rate. These results are similar to those described by Hocken[3] and fit with the 1980 AHA recommendations[2] which state that 'the larger bladder usually records systolic pressure in the thighs as higher by 10–40 mmHg than that in the arms, but the diastolic pressure is essentially the same'.

Mauck and his co-workers[7] used arterial segments in a partially fluid-filled chamber to show that the chamber pressure for maximum oscillation is strongly dependent on compression chamber volume, pulse pressure and arterial elasticity. The counter pressure for maximum oscillation always occurred between diastolic and true mean pressures. The volume ratio between the pressure chamber and the contained vessel governed this relationship. For small ratios, chamber pressure approximated to the mean and for larger ratios to the diastolic pressures. Extrapolating to *in vivo* measurements replacing chamber air volume with cuff volume, however, may well be unreliable. Nonetheless, it may provide an explanation for the differences between calculated and actual mean pressure data.

The AHA continues to recommend that the cuff-bladder width be 20% greater than the limb diameter or 40% of the limb circumference. A bladder width/limb circumference ratio of 0.4 to 0.6 was used by Hutton and his colleagues in 1984 and this ratio was also determined in this study.[1] The ratios for arms fell between 0.4 and 0.6, whereas for all thighs the ratio was less than 0.4 using the cuffs supplied by the manufacturers. Substituting thigh dimensions into the above ratio, the predicted width of the cuff should have been at least 25 cm for some of the patients.

The practical implication of these results is that an anaesthetist who has access only to the thigh, can use the MAP and the pulse rate as displayed. The thigh SAP and DAP are different from the arm values and a correction based on Figs 1 and 2 should be applied. The measured and calculated MAPs are highly significantly different in the arm but not in the thigh data, although both are highly correlated. This corresponds to our normal understanding of mean arterial pressure, but only applies in the thigh.

The multiple regression analysis results suggest that measured MAP depends on the site of measurement. If SAP = 120 mmHg and DAP = 80 mmHg, then on conventional calculations MAP would be 92.8 mmHg. The multiple regression equations, which describe the way the Dinamap functions, predict arm MAP = 94 mmHg and 94.41 mmHg for the thigh. For all practical purposes these differences are unimportant.

Acknowledgments

The authors gratefully acknowledge the assistance of the Recovery Room staff in the Vale of Leven Hospital and also wish to thank Mrs B. Docherty for her careful typing.

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Anaesthesia, 1986, Volume 41, pages 1036–1038

APPARATUS

Pulse oximetry

An assessment in anaesthetised dental patients

M. C. C. CLAPHAM AND A. M. MACKIE

Summary

The applications of a pulse oximeter were studied in dental day case surgery using nasal mask anaesthesia. Changes in arterial oxygen saturation were sensitively and rapidly detected, in the absence of cyanosis. Impaired oxygenation can be detected before cyanosis develops.

Key words

Measurement technique; pulse oximetry.
Anaesthesia; dental.

It is recognised that the detection of the desaturation of haemoglobin by observation for cyanosis is unreliable and varies between different observers.[1] It is conventionally claimed that cyanosis is only apparent when there are 5 g/dlitre of reduced haemoglobin. If the haemoglobin concentration is 15 g/dlitre it will not occur until the arterial saturation is 65% and the $Pa\text{o}_2$ 4.2kPa. A new generation of pulse oximeters[2] is now available, which have the potential ability to measure arterial saturation continuously and noninvasively. A device which gives early warning of minor degrees of desaturation before cyanosis is apparent, is immediately attractive.

This study was designed to examine the performance and convenience of the BTI Biox III (Ohmeda) oximeter in patients anaesthetised for outpatient dental surgery without tracheal intubation.

Apparatus

In the BTI Biox III a lightweight probe is clipped to the earlobe or finger. The probe generates red and infrared light beams, alternated many times each second. Their relative transmission through tissue is detected by a photoelectric cell. The signal generated is modulated by the pulsatile flow of arterial blood. Processing of this signal permits calculation and display of the arterial haemoglobin oxygen saturation ($Sa\text{o}_2$) and is not influenced by venous saturation or skin pigmentation. The previous generation of oximeters gave only a mean figure for the tissue's transmission, so the saturation reading was affected by other variables.

Noninvasive pulse oximetry has been compared with direct measurements of $Sa\text{o}_2$ in arterial samples from volunteers and patients in intensive care units.[3,4] The two methods give results that are closely comparable, indicating that pulse oximetry gives a satisfactory measure of $Sa\text{o}_2$ in the steady state.

Methods

Forty-seven outpatients presenting for dental extractions were studied. Induction of anaes-

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thesia was with intravenous thiopentone in 41 patients and by inhalation of oxygen, halothane and nitrous oxide in six. In all cases maintenance was with oxygen (30–35%), halothane and nitrous oxide, administered by nasal mask. During surgery a mouth prop was introduced, followed by a throat pack to protect the airway from debris and to minimise mouth breathing. The oximeter's ear probe was applied prior to induction, except in some of the smaller, anxious children. The lowest Sao_2 observed during each minute from induction to recovery and the inspired oxygen concentration were recorded. To avoid influencing the anaesthetic technique in this preliminary study, the anaesthetist was only informed of the Sao_2 if it fell below 85%. Relevant events (episodes of airway obstruction and cyanosis) were noted.

Results

The 47 patients studied comprised 22 females and 25 males; the mean age was 9.9 years, range 2–52 years). They received 352 aggregate minutes of anaesthesia from induction to completion of surgery. The frequency distribution of minimum saturation is displayed in Fig. 1. The saturation fell below 90% in 28 patients and below 85% in nine patients. The minimum saturation recorded was below 90% in 84 minute periods, below 85% in 22 minute periods and below 75% in only one minute period.

Three patients, aged 8, 10 and 12 years, developed clinical cyanosis. In all three the development of cyanosis was preceded by a similar sequence of saturation changes. This was a saturation below 90% for 2 consecutive minutes followed by a further rapid decrease in saturation to 76% in two cases and 68% in one case.

Discussion

The apparatus proved simple and convenient to use and was well accepted by the patients, anaesthetists and surgeons. The probe needed reapplication subsequent to displacement on a few occasions.

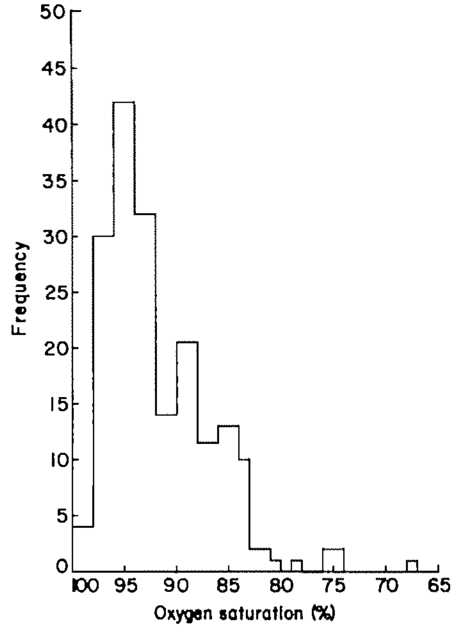

Fig. 1. Frequency distribution of the lowest oxygen saturation recorded during each minute period of anaesthesia.

During 22 minute periods of anaesthesia, in nine patients, Sao_2 was observed to be less than 85% and the anaesthetist was informed. Three patients went on to become cyanosed; in all these cases, the investigator had been able to warn the anaesthetist that a further rapid decrease in saturation was occurring before the cyanosis became apparent. Thus, the oximeter often revealed small degrees of desaturation, but more importantly, always gave earlier warning of the development of significant desaturation than the observation of cyanosis alone. This was also true in patients with pigmented skin.

The use of pulse oximeters in intensive care[4] and specialised situations such as one lung anaesthesia[5] has been reported. In this study, we found the device simple and reliable in everyday dental anaesthesia. However, during assessment in general surgery, the use of diathermy interfered with Sao_2 measurement and activated the alarm.

In conclusion, therefore, continuous measurement of arterial haemoglobin oxygen saturation must contribute to patient safety during general anaesthesia.

Acknowledgments

The authors would like to thank Ohmeda for the loan of the Biox III oximeter.

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SPECIAL ARTICLE

Some aspects of epidural block provided for elective Caesarean section

J. S. CRAWFORD, P. DAVIES AND M. LEWIS

Summary

We present here clinical data from 993 patients who were destined to undergo elective Caesarean section under epidural analgesia. In 29 cases the attempt to provide an epidural was abandoned before the operation started. In regard to this, the importance of monitoring the fetal heart rate during initiation of the epidural is emphasised. In 10 cases general anaesthesia was induced after delivery, and in a further 108 cases supplemental analgesia was administered, either systemically, by inhalation or by an additional epidural top-up, after delivery. Satisfactory analgesia throughout the operation was achieved in 87.8%. In an appreciable proportion of cases the recommended maximum dose of bupivacaine, and the recommended maximum rate of bupivacaine administration, were exceeded without apparent complication. There was a tendency for the volume of Hartmann's solution infused intravenously before and during initiation of the epidural to be increased throughout the period under review (1971–85). The prevalence of hypotension diminished during that period. Characteristics of the data did not permit a close analysis of the main factors which could have led to an episode of maternal hypotension. However, it did appear that such an episode could be ascribed to too brief an interval between the first and second, or the second and third top-up doses. The frequency with which blood was transfused during operation was markedly lower than that noted in a concurrent series of elective sections conducted under general anaesthesia. Brief reports of six unusual complications are included and attention is drawn to the prominence of the use of 0.75% bupivacaine in these, and also to the frequency with which use of that solution was associated with unsatisfactory analgesia.

Key words

Anaesthesia; obstetric.
Anaesthetic techniques, regional; epidural.

Epidural analgesia for Caesarean section has become an increasingly popular maternal choice in the United Kingdom during the last decade. The generally advocated technique of its administration has been gradually modified during that period, in the light of clinical experience. The most notable areas of change have been in the extent of preloading the circulation, the identity, concentration and volume of local anaesthetic used and the pattern of administration of the total volume administered.

This paper is a review of our experience of 993 consecutive cases of elective section conducted since 1971 (prior to this an epidural had been provided for very few elective sections in this hospital), with particular regard to the factors

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referred to above and to the maternal responses. Also included are brief accounts of six of the 993 cases which we believe merit particular consideration. The report thus complements our account of complications of epidural analgesia provided for labouring women.[1]

This is not a rigorously scientific analysis of the responses to, and the consequences of, lumbar epidural analgesia provided for elective Caesarean section. It is an account of the experience of this technique culled from the clinical data accumulated in one hospital service. It is hoped that by demonstrating the frequency of occurrence of noteworthy blemishes of the technique, and by identifying the factors which appear to be most frequently associated with those defects, other clinicians will be afforded worthwhile information which will be of help in their efforts to enhance further the safety and effectiveness of this method of analgesia within their own clinical practice.

Methods

The following were recorded for each of the cases: year of administration, volume of balanced electrolyte solution infusion for preloading, volume and composition of each injection into the epidural space, (excluding the 2 or 3 ml plain lignocaine 1% frequently used as a test dose), time elapsing between repeat administrations, time from final dose to delivery, total volume of local anaesthetic solution injected, total mass of bupivacaine injected and requirement to provide additional analgesia during operation. Whether or not the attempt to provide an epidural was abandoned was recorded, as was the posture of the mother at the time of each injection. The incidence of hypotension was noted and if it occurred, whether this was treated by administering either ephedrine or atropine, or whether it responded simply to a change of maternal posture and/or an increased rate of infusion of Hartmann's solution. The requirement for blood transfusion intra-operatively was also noted.

In a few cases some items of information were missing from the records. This should be borne in mind when considering apparent discrepancies in the Tables as presented. Because of the heterogeneity of this series, we have not considered it to be sensible to relate any of these factors to the clinical condition of the infant at birth.

Results

Agent used

Bupivacaine only was employed in 989 cases, etidocaine only in three and in one only chloroprocaine was administered.

Efficiency of analgesia

This has been assessed on the basis of a requirement to provide supplementary analgesia. Thus, instances of a rather frequently occurring brief episode of substernal discomfort experienced during delivery, or more often, immediately after, are not considered.

In 29 cases, general anaesthesia was induced before delivery. Attempts to provide an epidural for the operation were abandoned either because of failure to achieve an adequate sensory block, or because of evidence of maternal or fetal distress. In each of these cases the agent used was bupivacaine. In 20 cases the concentration of the top-up dose preceding the decision to abandon the procedure was 0.5% plain, in one case 0.5% with adrenaline and in eight cases 0.75%.

General anaesthesia was resorted to post-delivery in 10 cases because of maternal distress. In a further 64 cases an additional epidural top-up was administered after delivery. Supplementary analgesia was provided, either systemically or by inhalation, or both, after delivery to an additional 49 mothers, of whom five also received an epidural top-up and are included in the 64 cases previously mentioned. Thus, of the 964 patients who were in receipt of an epidural, at least to the time of delivery, 846 (87.8%) required no additional analgesia. The rates have been reasonably constant during the period under review (Table 1). The requirement for post-delivery analgesia did not appear to be related to the mean dose of bupivacaine administered.

Fluid regimen

Each patient received an intravenous infusion of Hartmann's solution. The term 'preloading', as used here, is a misnomer, because the volume referred to includes not only that given before the start of the epidural, but also that infused up to, roughly, the start of operation.

The mean volume so infused has increased markedly during the period under review. Thus from 1971–77 it was 1357 ml (SD 477), from

Table 1. Number of cases in which general anaesthesia was administered before the start of operation and, among the remainder, percentage incidences of the provision of analgesia additional to the preparatory epidural, categorised by the years under review. Also noted is the mean mass of bupivacaine administered to the patients categorised according to their required postdelivery analgesia

Period (no.)	GA pre-delivery (no. of cases)	Percentages of cases excluding GA pre-delivery: GA post-delivery	Supplementary epidural	Systemic and/or inhalational	No additional analgesia
1971–77 (73)	1	2.8	0	9.7	87.5
1978–81 (309)	14	1.0	6.8	3.4	88.8
1982–85 (611)	14	0.8	7.4	4.5	87.3
Mean mass (mg) of bupivacaine administered		212.2	144.3	190.0	169.6

Table 2. Number of occasions upon which each of the bupivacaine solutions was used for each of the indicated top-ups among 989 patients, and mean volume of bupivacaine solution used for each successive top-up

Bupivacaine solution	Sequential number of top-up: 1	2	3	4	5	6	7–9	Total
0.25%	0	0	8	8	4	2	1	23
0.375%	2	0	1	1	3	0	0	7
0.5% plain	758	730	624	352	140	44	17	2463
0.5% + adrenaline	56	57	47	28	10	2	0	200
0.75%	173	171	148	71	24	12	6	605
Total	989	958	828	460	181	60	24	3298
Mean vol (ml)	10.16	9.03	8.00	7.18	6.99	6.97	7.12	
(SD)	(3.33)	(2.08)	(2.55)	(2.68)	(2.79)	(2.92)	(3.18)	

1978–81 it was 1533 ml (SD 440) while from 1982–85 it had increased to 1852 ml (SD 579). The number of patients involved in these respective periods were 61, 307 and 611.

Dosage of local anaesthetic

From here on only those 989 cases in which bupivacaine was the only local anaesthetic administered will be considered. The drug was administered in a variety of modes; the choice was not necessarily constant for any one patient.

The total number of top-ups received by the individual patient ranged between one and nine and the number of occasions on which each solution was used for each top-up is shown in Table 2. There was a marked increase during the period reviewed in the mean number of top-up doses given per patient (Fig. 1). Over the entire period, the mean volume of solution of bupivacaine injected tended to be reduced with successive top-ups (Table 2).

The average mass of bupivacaine administered per mother also increased during the period under review (Table 3), although the mean volume of

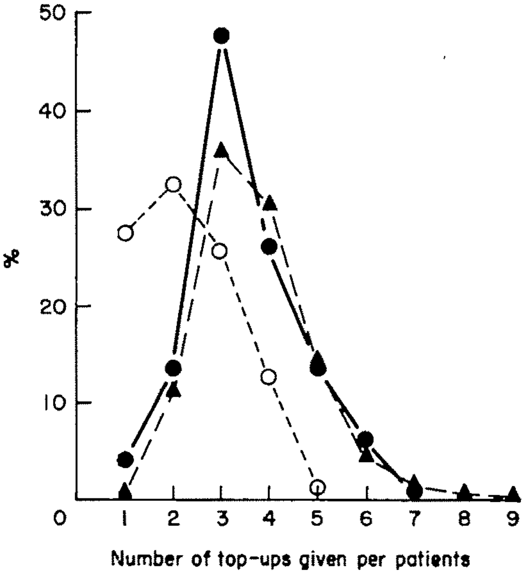

Fig. 1. Percentage incidence of patients who received the indicated number of top-ups, within the designated periods. ○---○, 1971–77; ●—●, 1978–81; ▲—▲, 1982–85.

Table 3. Mass of bupivacaine, volume of bupivacaine solution, time elapsing between first and last top-up, administration rate of mass of bupivacaine and of solution of bupivacaine. Excluded from this analysis are cases in which general anaesthesia was induced before the start of operation and those in which only one dose of bupivacaine was given before delivery

Years (*n*)	Mass (mg) mean (SD) (range)	Volume (ml) mean (SD) (range)	Interval (minutes) mean (SD) (range)	Mass/min mean (SD) (range)	Volume/min mean (SD) (range)
1971–77	121.9 (39.3)	26.4 (7.8)	40.5 (35.1)	5.1 (3.8)	1.02 (0.78)
(52)	(70–311)	(14–55)	(5–204)	(1.3–20.0)	(0.2 – 4.0)
1978–81	162.5 (50.0)	32.7 (9.9)	49.7 (30.3)	4.3 (2.7)	0.86 (0.54)
(290)	(50–400)	(10–80)	(5–195)	(0.6–29.0)	(0.2 – 5.8)
1982–85	177.3 (68.1)	31.0 (9.6)	49.9 (30.6)	4.5 (2.6)	0.78 (0.37)
(594)	(40–555)	(10–80)	(5–221)	(0.9–21.4)	(0.2 – 2.9)

solution injected did not rise during the second half of the period. However, the mean rate of administration of bupivacaine and of the volume of the anaesthetic solution was lower from 1978 onwards, which reflected the fact that the time elapsing between administration of the first and the final top-up increased during the latter period. The average time from giving the final dose to delivery, excluding from consideration those cases in which general anaesthesia was given before delivery and those in which only one injection of bupivacaine was given prior to operation, also increased over the period. Thus, the times for the three periods 1971–77 ($n = 52$), 1978–81 ($n = 290$) and 1982–85 ($n = 594$) were, respectively, 34.4 minutes (SD 18.0), 39.7 minutes (SD 20.5) and 42.8 minutes (SD 18.7).

Single dose cases

Twenty-two mothers received only one dose of bupivacaine, without supplementary anaesthesia or analgesia, up to the time of completion of the operation. The mean volume of bupivacaine was 19.5 ml (SD 4.3, range 10–26 ml), and mean mass was 95.9 mg (SD 20.6, range 50–130 mg). The mean time taken from injection of the drug to the start of the operation was 57.3 minutes (SD 21.2, range 15–99 minutes).

Rate of administration and total dosage

The percentage of patients in the three designated periods (excluding those who were given only one dose) whose total received dose of bupivacaine was at least 150 mg were: 1971–77, 16%; 1978–81, 42%; 1982–85, 53%.

Assuming a maternal weight of 75 kg, the percentages, in the three periods, of those who received bupivacaine at a rate of at least 2 mg/kg/15 minutes were: 1971–77, 8%; 1978–81, 3%; 1982–85, 4%.

Hypotension

A hypotensive response to an epidural top-up cannot, in the context of this discussion, be sensibly defined with reference to a specific extent of fall of blood pressure. Some of the mothers included in this series had an antenatal systolic blood pressure of 190 mmHg, others of 85 mmHg. Here we have defined a hypotensive episode as having occurred when the anaesthetist has so identified it or when it is apparent, from the anaesthetic record chart, that it occurred. As a generalisation, hypotension is designated as having occurred in the healthy, normotensive mother, when the systolic blood pressure fell by at least 20 mmHg for more than a very brief period.

Among the 993 cases, an episode of hypotension occurred in 143 (14.4%). Two episodes of hypotension were recorded as having occurred in 16 of these cases (1.6%). A differentiation can legitimately be made between two types of hypotension: one in which the fall of blood pressure was promptly and successfully reversed by either changing the maternal posture or increasing the rate of intravenous infusion of Hartmann's solution (which we henceforth refer to as 'hypotension, no medication'), the other which, in the opinion of the anaesthetist, required the administration of either ephedrine or atropine (or both) to retrieve the situation (referred to as 'hypotension, medication'). The former can generally be considered relatively benign, the latter to be a more serious commentary upon the technique. In 60 cases (6.0%) pharmacological reversal of the fall of blood pressure was deemed to be necessary (on two occasions for each of six patients). Ephedrine alone was given once to 42 mothers and twice to five mothers; atropine alone was given to 11 mothers; ephedrine and atropine were given simultaneously to one, and at separate times to another. In 10 cases, two episodes of hypotension were relieved by postural change and increasing the rate of infusion.

The prevalence of hypotension during the latter half of the period reviewed was considerably lower than that previously encountered. Thus, the figures for the 'no medication' and the 'medication' groups in the three periods were, respectively, 16.9% and 12.7% for 1971–77, 8.5% and 3.6% for 1978–81 and 7.0% and 6.6% for 1982–85. This is not mirrored by a reduction in the total mass of bupivacaine injected, or by the total volume of solution of the drug used (each of which rose during the period), but the trend is paralleled by a reduction in the rate of administration of bupivacaine and by an increase in the mean time which elapsed between injection of the first dose and the final dose (Table 3).

Identification of the factors which might have made a major contribution to an episode of hypotension is bedevilled by the multiplicity of candidates. The composition of the injected solution can be of importance. The prevalence of hypotension when related to the latter variable was: hypotension with no medication 8.2% of 734 patients given 0.5% plain bupivacaine, 1.7% of 59 patients given 0.5% with adrenaline and 10.2% of 166 patients given 0.75% bupivacaine; the corresponding figures for hypotensive patients who required medication were 5.9%, 8.5% and 7.9%, respectively. In consideration of these figures it should be noted that the use of both 0.75% bupivacaine and of the adrenaline-containing solution was almost exclusively confined to the period since 1981 when, as previously observed, the mean volume of preloading was higher than that in the earlier periods.

Other factors that might be related to a hypotensive episode are the time elapsing between the last but one and last doses immediately preceding the hypotension, the volume of bupivacaine solution administered immediately before the episode and the overall rate of administration up to that point.

This study permits only tentative speculation about such factors. It is a marked feature of these data obtained from clinical practice that the greater the number of top-ups given, the lower the mean volume per dose. Thus, although the prevalence of hypotension was apparently higher among mothers who had received few doses, these mothers had also had a greater volume per dose than the remainder. Any consideration of the factors potentially associated with hypotension should, with these data, take into account whether the episode occurred early or late in the sequence of top-ups. We have chosen to compare those with, say, a first hypotensive episode at the third

Table 4. Rate of administration of bupivacaine solution (mean, SD) up to the time of occurrence of hypotension, which was corrected either by a change of maternal posture and/or increased rate of intravenous infusion ('no medication') or by administering ephedrine or atropine or both ('medication'), categorised in regard to the number of the top-up in the sequence. For comparison, the rate of administration among mothers who did not develop hypotension is detailed, grouped according to the number of top-ups given during the course of the procedure

Sequential number of top-up	No hypotension Rate to final dose ml/minute (*n*, SD)	Rate of dose at which hypotension first occurred ml/minute (*n*, SD)	
		No medication	Medication
2nd	1.27 (89, 0.59)	2.02 (23, 0.69)	2.51 (18, 1.52)
3rd	0.87 (335, 0.41)	1.00 (15, 0.47)	0.87 (18, 0.34)
4th	0.68 (266, 0.17)	0.53 (7, 0.18)	0.67 (6, 0.10)
5th	0.61 (115, 0.44)	0.67 (6, 0.10)	

top-up with those who had exactly three top-ups but who did not get hypotension. Though not strictly comparable, this seems the fairest method of defining groups whose treatment should have been potentially similar.

Of the factors mentioned above, the only apparent difference of note lies, as shown in Table 4, in the rates of administration preceding the top-up concerned. It would appear that those showing hypotension at an early stage had received substantially higher rates of administration prior to this episode than those who did not show hypotension.

Intra-operative blood replacement

The percentage frequency with which a blood transfusion was started during the operation fell by 50% during the second half of the period under review, compared with that during the first half. The contrast with the frequency of blood transfusion at elective section conducted under general anaesthesia in this unit during similar timespans is quite striking. Thus, the percentage of patients requiring blood transfusion under epidural or general anaesthesia in the three periods was, respectively, 5.5% and 13.0% in 1971–77, 2.3% and 8.2% from 1978–81 and 2.8% and 9.2% in the years 1982–85. There was no noteworthy difference related to the solution of bupivacaine used.

Unusual complications

Six patients developed complications which deserve comment.

Patient 1. The patient presented for elective section for moderate pre-eclampsia (weight 67 kg). Bupivacaine 0.5% plain in volumes of 8 + 8 + 8 ml were given over a period of 27 minutes. The start of the operation was delayed for 2 hours because of emergency commitments. Top-ups were recommenced and given as follows: 15 + 8 + 8 + 5 ml of 0.5% bupivacaine plain over a period of 40 minutes (180 mg bupivacaine at a rate of 4.5 mg/minute, approximately 0.9 mg/kg/15 minutes). A grand mal convulsion occurred shortly after the final dose. She was immediately turned to the full left lateral position and tracheal intubation performed using thiopentone and suxamethonium. There was no hypotension (blood pressure 160/105), or evidence of fetal distress. The operation was conducted under general anaesthesia, and the infant was in excellent condition at delivery. There were no related maternal ill effects.

Patient 2. The mother (weight 64 kg) was not an epileptic and was not suffering from pre-eclampsia. Top-ups with 0.75% bupivacaine were 10 ml + (15 minute interval) 10 ml + (26 minute interval) 5 ml + (19 minute interval) 10 ml + (23 minute interval) 10 ml + (35 minute interval) 6 ml. She therefore received 382.5 mg bupivacaine at a rate 4.61 mg/minute, approximately 0.9 mg/kg/15 minutes). A grand mal seizure lasting for 20 seconds occurred 6 minutes after the final dose, as she was being transferred to the operating theatre. No hypoxaemia or hypotension were noted. The operation was conducted under the epidural, and the mother and baby remained well. The concentration of bupivacaine in maternal venous blood sampled shortly after convulsion was 2.5 μg/ml plasma, and in umbilical vein blood it was 0.9 μg/ml plasma.

Patient 3. This patient was undergoing a repeat Caesarean section (weight 83 kg). Top-ups were with 0.75% bupivacaine 10 + 10 + 10 ml over a period of 48 minutes (225 mg bupivacaine, rate 4.68 mg/minute, approximately 0.9 mg/kg/15 minutes). The mother was very drowsy throughout the operation and for the subsequent hour, but showed no other disquieting signs or symptoms. The infant was in excellent condition at birth.

Patient 4. The patient was a 39-year-old primigravid (weight 68 kg), with hypertension plus drowsiness from 16 weeks gestation and proteinuria from 32 weeks. An initial dose of 3 ml 0.5% bupivacaine plain was followed 8 minutes later with 10 ml 0.75% bupivacaine, which was very shortly followed by a convulsion. General anaesthesia was subsequently induced and the baby was in good condition at delivery. A diagnosis of eclampsia was made. The maternal blood pressure began to rise during the early part of the operation and an infusion of hydralazine was started. There were no sequelae of the convulsion.

Patient 5. This patient was given 70 ml of 0.75% bupivacaine in 10 ml increments (525 mg bupivacaine, at a rate of 8.75 mg/minute, approximately 1.75 mg/kg/15 minutes). Difficulty with vision and a bilateral Horner's syndrome developed shortly after the final dose. The mother (weight 74 kg) evidenced slurred speech and some confusion. There was a moderate fall of blood pressure, from a maximum systolic of 120 mmHg to a minimum systolic of 95 mmHg, of fairly brief duration. No other ill effects occurred and the infant was in excellent condition at delivery.

Patient 6. The patient presented for repeat Caesarean section (weight 110 kg, aged 42 years). Injection of 5 ml of 0.75% bupivacaine was followed by a prolonged period of severe hypotension. This was treated with rapid infusion of 2 litres of Hartmann's solution and two intravenous injections of ephedrine 15 mg. Her condition stabilised, and 15 minutes later 5 ml 0.5% bupivacaine was given through the same catheter with no untoward response. The start of the operation was delayed for an unrelated reason. Delivery, 58 minutes after the second dose of bupivacaine was of an infant in excellent condition clinically and biochemically. No related maternal sequelae to the hypotensive episode occurred and there was no spinal headache.

Total failures

Two of the cases in which general anaesthesia was given before delivery are referred to in the previous section.

In seven cases the sensory block could not be extended above T_{10}; two of these mothers had severe pre-eclampsia, which prompted early abandonment of attempts to extend the block. Entry into the epidural space could not be gained in five cases; in one of these, fetal bradycardia developed and the prompt administration of general anaesthesia was considered to be advisable. In two other cases evidence of fetal distress led to abandonment of attempts to provide an epidural. In one, maternal hypotension preceded the fetal bradycardia (two doses of 5 ml 0.5% bupivacaine plain had been given), while in the other there was no accompanying maternal complication (8 ml 0.5% bupivacaine plain had been followed, 30 minutes later, by 12 ml of the same solution).

In seven patients (with re-insertion of the catheter in one) no evidence of nerve block could be obtained, despite repeated top-ups. One of these was subsequently a case of 'failed intubation'! Patchy distribution of sensory block led to abandonment of the attempt in five cases. Interestingly, in four of these cases, the solution injected was 0.75% bupivacaine. One mother became very anxious and agitated as the epidural block developed and, as a result of mutual agreement, she was given a general anaesthetic.

Discussion

This is, as stated earlier, a review of clinical experience. It would be unrealistic to expect it to provide the form of precise and detailed information obtainable from a prospectively conducted research project. However, certain generalisations of interest can be discussed.

The incidences of total and partial failure to provide satisfactory analgesia approximate closely to those relating to epidural analgesia provided for labour in our practice: 2.5% total failure (excluding those cases in which the epidural catheter was sited too late to provide analgesia) and in 12%, partial failure due to missed segment, unilateral relief or inadequate sacral block. The reason for a total failure varied. In 24 cases it was related to a failure to achieve an effective block. It is of interest that patchy distribution of the sensory block was encountered in four of the 173 cases in which 0.75% bupivacaine was used, and in only one of the remainder. It is also worthy of note that evidence of fetal distress led to the abandonment of attempts to initiate an epidural in three cases, which underlines the importance attached to the requirement that external monitoring of the fetal heart rate must be in progress from before the mother is placed into the appropriate position, until she is ready to be transported to the operating theatre.

The advisable limits of safety relating to the administration of bupivacaine remain a matter of some contention. The manufacturers[2] advise that the rate of administration should not exceed 2 mg/kg/15 minutes and that the total dose within a reasonable period should be no greater than 150 mg. Moore *et al.*[3] suggested that these limits were too stringent, but other authorities[4,5] have supported their observance. In the current series the advised rate of administration was exceeded in 4% of cases, yet in the four cases in which central nervous system (CNS) toxicity could have been deemed to have become evident, the rate of administration was less than half the suggested maximum. The total dose exceeded 150 mg in 47% of the cases, but in only four did signs of CNS toxicity become manifest. It is noteworthy, however, that in four of the five cases identified as having exhibited signs of CNS toxicity, 0.75% bupivacaine had been administered. Our results suggest that there is a wider margin of safety than the manufacturers, with commendable caution, have advised, when 0.5% bupivacaine is administered. It would, however, be presumptuous and inappropriate for us to suggest an advised maximum on the basis of such a review.

The frequency of an episode of hypotension during the latter half of the period under review was less than half of that previously encountered. It appears that this was, in part at least, the result of two modifications in practice: an increase in the volume of infused fluid before and during establishment of the block and an increase in the interval between top-ups. In the entire series, rather more than half of the episodes of hypotension responded favourably to a change in maternal posture and/or an increased rate of infusion of Hartmann's solution. In only one case was the episode of maternal hypotension accompanied by evidence of fetal distress.

An episode of hypotension was more likely to occur earlier in the establishment of a block than later. This was possibly related to the fact that the volume of bupivacaine solution injected tended to be decreased with succeeding top-ups. However, of possibly greater significance is the observation that the mean rate of administration of the drug early in the sequence of top-ups was approximately 2.0 mg/kg/15 minutes in the 'hypotension, no medication' group, and approximately 2.5 mg/kg/15 minutes in the 'hypotension, medication' group, that is, equal to or exceeding the advised maximum. Perhaps the conclusion to be drawn is that prolongation of the interval between the first two or three top-ups is more important to the safety of the procedure than is limitation of the total dose and of the overall rate of administration.

That the frequency of intra-operative blood transfusion was considerably less in the epidural series than in our series of 2203 elective sections conducted under general anaesthesia was gratifying, but remains somewhat puzzling to us. The difference did not, apparently, reflect an overwhelming dominance in the general anaesthesia group of cases in which excessive blood loss could reasonably be anticipated. It is doubtful that the anaesthetists concerned were markedly reluctant to start a blood transfusion in an awake patient. The distinction might concern the fact that under epidural analgesia myometrial tone is well sustained, whilst the volatile anaesthetic agents (trichloroethylene, methoxyflurane and halothane) employed in the great majority of cases conducted under general anaesthesia tend, to a greater or lesser extent, to relax the uterus. However, it is certainly not our experience that the obstetrician requests that the mother be given a uterine relaxant any more frequently when an epidural is being used than when general anaesthesia is in progress. Most of the blood loss at Caesarean section is from the uterus, so it would be interesting to pursue this question.

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Anaesthesia, 1986, Volume 41, pages 1047–1049

Forum

Effects of atracurium on intracranial pressure in man

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Summary

Intravenous administration of 0.6 mg/kg of atracurium to nine patients did not produce any significant change in intracranial, mean arterial or cerebral perfusion pressures. In another three patients, anaesthesia was induced with thiopentone 5 mg/kg after muscle relaxation with atracurium 1 mg/kg. Intracranial pressure was below pre-induction levels in two patients whose tracheas were intubated 90 seconds after atracurium. The vocal cords were not fully relaxed at 90 seconds in the third patient. Intubation at 150 seconds in this patient was associated with a rise in intracranial pressure above pre-induction values.

Key words

Anaesthesia; neurosurgical.
Neuromuscular relaxants; atracurium.

Although the use of atracurium for neurosurgical procedures has been reported,[1] until recently its effect on intracranial pressure (ICP) was not clear. The present study, undertaken before the report of Minton *et al*,[2] was aimed at evaluating the effect of atracurium on ICP, mean arterial pressure (MAP) and cerebral perfusion pressure (CPP) and to see if this agent has any advantages over pancuronium for the induction of anaesthesia in patients undergoing intracranial surgery.

Methods

Twelve adult subjects scheduled for craniotomy or shunt operations were studied. All had normal levels of consciousness and informed consent was obtained during the pre-operative visit. They were divided into two groups.

Group 1. Five subjects with intracranial space-occupying lesions were premedicated with 10 mg of oral diazepam approximately 90 minutes before induction of anaesthesia. After performing arterial and venous cannulation, anaesthesia and muscle relaxation were induced with thiopentone and pancuronium and, following tracheal intubation, maintained with nitrous oxide, oxygen and 3 μg/kg of fentanyl. A ventricular catheter was inserted into one of the lateral ventricles through a small burr hole to measure ICP. The end tidal $P\text{CO}_2$ was allowed to rise above 4.0 kPa and $P\text{aCO}_2$ was monitored to ensure that the value was maintained between 4.5 and 6.5 kPa. After 5 minutes of control measurements, 0.6 mg/kg of intravenous atracurium was administered and the ICP, arterial pressure and end tidal $P\text{CO}_2$ were recorded continuously over the next 10 minutes.

Another four subjects scheduled for shunt operations were anaesthetised as above, but the arterial pressure was measured indirectly with a Dinamap. ICP measurements were commenced only after the ventricular end of the shunt operation was completed. A Cordis ventricular catheter was inserted and the operation was stopped until the end of the study.

Group 2. Three subjects with intracranial space-occupying lesions, who had pre-operative ICP monitoring had anaesthesia and muscle relaxation induced with 1 mg/kg of atracurium followed by 5 mg/kg of thiopentone. Tracheal intubation was attempted at 90 seconds after atracurium. ICP and arterial pressure were measured continuously during the induction of anaesthesia.

Student's *t*-test was used to test the significance of differences between values; a difference was considered

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Table 1. Mean (SEM) values for ICP, MAP, CPP and $P\text{E}'\text{CO}_2$ during control period and at 1, 3, 5, 7 and 10 minutes after atracurium in Group 1 patients

	Control	1 minute	3 minutes	5 minutes	7 minutes	10 minutes
ICP	10	11	10	10	10	10
(mmHg)	(1.08)	(1.20)	(1.28)	(1.21)	(1.33)	(1.29)
MAP	87	85	85	85	84	85
(mmHg)	(3.99)	(3.93)	(3.67)	(4.10)	(4.10)	(4.27)
CPP	76	74	74	75	74	75
(mmHg)	(3.90)	(3.74)	(3.99)	(3.99)	(3.90)	(4.04)
$P\text{E}'\text{CO}_2$	4.3	4.3	4.4	4.4	4.4	4.4
(kPa)	(0.14)	(0.14)	(0.14)	(0.15)	(0.15)	(0.15)

significant when the value for p was less than 0.05.

Results

Table 1 shows the mean control values (SEM) for ICP, MAP and CPP (MAP − ICP) and end tidal $P\text{CO}_2$ as well as at 1, 3, 5, 7 and 10 minutes after atracurium in group 1 patients. The changes in the values after atracurium are not statistically significant.

Table 2 shows the values for ICP and MAP during the control period and at 60, 90, 120 and 180 seconds after the administration of atracurium in two patients in group 2, who were intubated at 90 seconds. In both, the ICP fell after thiopentone and showed a small rise during tracheal intubation; this was not above pre-induction control values. Figure 1 shows the ICP and arterial pressure tracing of a patient in Group 2, whose vocal cords were not well relaxed at 90 seconds and hence who was intubated only at 150 seconds after atracurium. In this patient, although the ICP did not rise above control values during the first laryngoscopy, it was well above the pre-induction levels during tracheal intubation.

Discussion

Before the introduction of any new drug into neuroanaesthetic practice, it is important to see whether the drug has any adverse effect on ICP, MAP and CPP. The present study shows that atracurium does not cause a rise in ICP in patients with intracranial space-occupying lesions and thus confirms the recent work of Minton and his colleagues.[2]

Certain drugs like droperidol may have no adverse effect on ICP,[3] but their hypotensive effect could reduce the MAP without a parallel fall in ICP, thereby causing a reduction in CPP. Histamine release by neuromuscular blocking agents could lead to severe hypotension. This seems to be the reason for the severe fall in CPP reported by Moss and his colleagues,[4] who used tubocurarine and thiopentone or Althesin for the induction of anaesthesia in patients with intra-

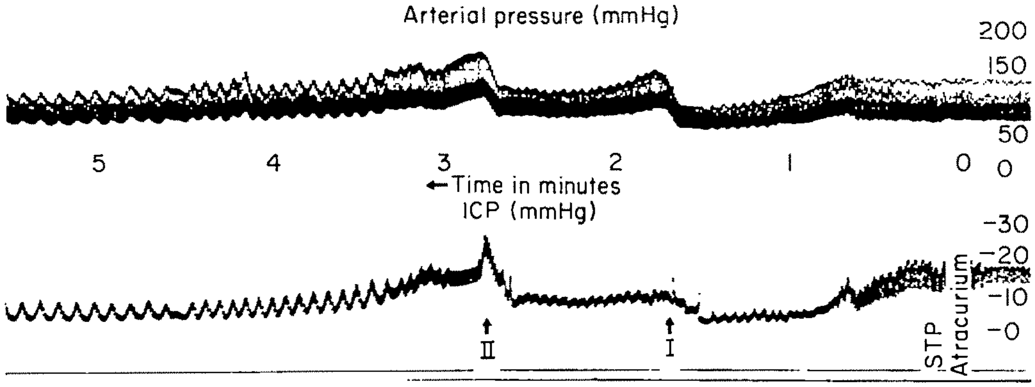

Fig. 1. Arterial and intracranial pressure tracing of a patient in Group 2 induced with atracurium and thiopentone (STP). Attempt at intubation at I abandoned as vocal cords were not fully relaxed. Intubated at II.

Table 2. Values for MAP and ICP at pre-induction (control) as well as at 60, 90 (intubation), 120 and 180 seconds after atracurium in two patients in Group 2

	MAP (mmHg)					ICP (mmHg)				
Serial no.	Control	60 seconds	90 seconds	120 seconds	180 seconds	Control	60 seconds	90 seconds	120 seconds	180 seconds
1	100	85	105	100	100	16	9	14	10	10
2	90	85	110	105	100	23	12	14	14	12

cranial tumours. Although we did not record any fall in MAP in our patients, histamine release[5] and hypotension[6] have been reported after the administration of atracurium.

A rise in ICP and MAP during tracheal intubation has been well documented. Unni *et al.*[7] have shown that a second dose of thiopentone, 30 seconds prior to laryngoscopy could attenuate ICP changes without a significant fall in MAP. A second dose of thiopentone was necessary as the conditions for intubation were not ideal before 3 minutes after pancuronium. Since the onset of neuromuscular block is more rapid, patients could be intubated earlier with atracurium than with pancuronium.[8] In the present study, it was possible to intubate two patients 90 seconds after atracurium followed by thiopentone without a clinically significant rise in ICP. However, relaxation of the vocal cords was incomplete at 90 seconds in the third case and this patient showed a much larger rise in ICP when intubated 1 minute later.

Acknowledgments

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Anaesthesia for transoral craniocervical surgery

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Summary

Transoral surgery on lesions in the craniocervical region has been performed on 25 patients in this unit. The anaesthetic management is presented. Tracheostomy and nasotracheal intubation have both been used. Peroperative monitoring of cord compression remains an important and only partly solved problem. There were two deaths as a result of anaesthesia and surgery, and these are discussed.

Key words

Anaesthesia; neurosurgical.

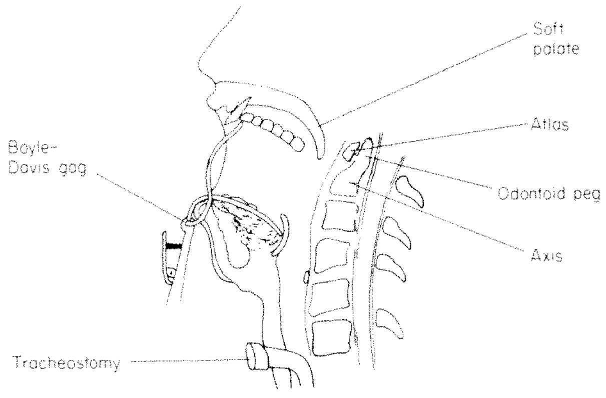

Fig. 1. Diagram in the sagittal plane with Boyle-Davis gag in place, illustrating the surgical approach.

The transoral route provides good surgical assess to the anterior craniocervical region (Fig. 1). It is particularly useful for relief of spinal cord compression in rheumatoid atlanto-axial subluxation[1] (Fig. 2), and in removal of intra- and extradural tumours.[2] Unfortunately, the high incidence of postoperative complications[3] has previously discouraged its use.

The main difficulties encountered are those of anaesthetising patients with atlanto-axial instability and of airway management. Other problems include wound and chest infection and the possibility of intra-operative cord compression. There are operative hazards associated with both transoral and conventional surgery in the craniocervical region. The relatively high mortality of conventional surgery,[4] together with recent advances in transoral surgical technique,[2] make it likely that the transoral route will become increasingly widely performed.

Between 1983 and 1985, 25 patients underwent this type of surgery in this unit. We have reviewed their anaesthetic management and postoperative course.

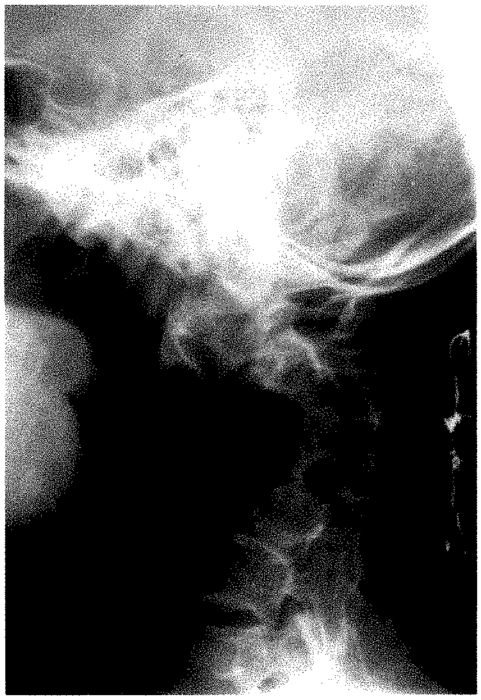

Fig. 2. Lateral radiograph of the neck from a patient with severe rheumatoid arthritis with symptoms of cervical myelopathy. Previous posterior fusion had been unsuccessful.

Patients and surgical technique

The mean age of the patients was 51 years (range 18–73). The indications for surgery are given in Table 1. Five patients were taking steroids and seven others were taking drugs causing immunosuppression (gold, azathioprine or penicillamine).

Table 1. Indications for surgery

Primary tumour	2
Metastasis	2
Syringomyelia	2
Rheumatoid arthritis	15
Platybasia	1
Trauma	1
Congenital bone dysplasia	2

All patients had transoral anterior decompression.[5] Access was achieved by using a Boyle-Davis gag and by retraction or splitting of the soft palate. A midline pharyngeal incision was made and an air drill used to remove the arch of the atlas, odontoid peg and clivus.

In addition, 19 patients had posterior craniocervical fusion by interlaminar wiring and bone grafting. Initially, the patients were supine for the anterior decompression and then turned prone for the fusion. Latterly, we used the 'park bench' position for both parts of the operation, so that the fusion could be performed before the patient was moved.

Anaesthetic technique

Premedication. Ten patients received sedative premedication of either a benzodiazepine or an opiate. In addition, six patients received hyoscine intramuscularly. Intramuscular or intravenous dexamethasone was given to all patients at induction of anaesthesia.

Induction of anaesthesia and airway management. Originally, anaesthesia was induced with thiopentone, followed by suxamethonium and oral intubation. A tracheostomy was then performed and a polyvinyl chloride (PVC) cuffed tracheostomy tube inserted. In the last eight patients, in an attempt to avoid tracheostomy, after thiopentone and suxamethonium, Moffett's* solution was dripped into the nostril and a cuffed armoured PVC nasotracheal tube passed under direct vision. This remained in place in the postoperative period.

Throughout induction and intubation, the neck was held in a neutral position, with avoidance of neck flexion and allowance of only minimal extension. Intubation was difficult in six patients. In two of these, difficulty had been anticipated before induction and anaesthesia was induced by spontaneous inhalation of halothane and oxygen. This allowed intubation to be achieved in one patient, but the other had severe limitation of mouth opening due to rheumatoid temporomandibular joint disease and intubation was impossible under direct vision or by the 'blind' method. A tracheostomy was performed while anaesthesia was maintained via a facemask. The mandible was then divided to allow surgical access. In the remaining five patients, difficulty had not been anticipated preoperatively.

A 12 French gauge nasogastric tube was passed in all patients.

Maintenance and monitoring. All patients were paralysed with tubocurarine and their lungs ventilated with 50% nitrous oxide in oxygen with halothane supplementation. A variety of analgesic supplements were also given. A 14-G peripheral intravenous infusion was instituted and the radial artery cannulated to allow direct blood pressure monitoring and regular blood gas analysis. The electrocardiogram and end tidal CO_2 were also monitored continuously. Heat loss was minimised by the use of a heated water mattress and metal foil blanket. Particular attention was paid to the arterial blood pressure during tightening of the interlaminar wires. Figure 3 demonstrates the transient changes in blood pressure which occurred during the final tightening of the wires in one patient. A more profound and persistent hypotensive response was seen in the patient with diaphyseal aclasia.

The mean duration of surgery was 5.3 hours (range 3–8 hours).

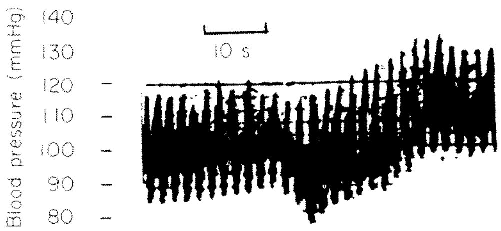

Fig. 3. Blood pressure recorded during surgery. Compression of the cord caused a sudden fall in blood pressure. Spontaneous recovery occurred when cord compression was relieved.

Postoperative management. The lungs of 11 patients were ventilated postoperatively. The mean postoperative ventilation was 27 hours (range 2–72 hours). Patients whose lungs were ventilated were sedated with an intravenous infusion of morphine or phenoperidine and two patients were given muscle relaxants. Nasotracheal tubes were removed after an average of 4 days and tracheostomy tubes were removed after an average of 7 days.

In order to minimise soiling of the pharyngeal wound with regurgitated gastric contents, the nasogastric tube was aspirated regularly and cimetidine and metoclopramide were given. When bowel sounds returned, nasogastric feeding was commenced, and the nasogastric tube remained *in situ* for 5 days. An infusion of intravenous pethidine or morphine was used to relieve postoperative pain in spontaneously breathing patients for 48 hours. Patients were also given dexamethasone and broad spectrum antibiotics.

Complications

Mean blood loss was one litre, although a displaced vertebral artery was damaged during surgery in one patient and four litres were lost rapidly. On one occasion, the pilot tube of the tracheal tube was damaged during intra-oral manipulation, causing cuff deflation. Re-intubation was deemed to be too hazardous because of the pharyngeal bleeding and swelling and tracheostomy was performed.

Five of the 17 patients who had tracheostomies before surgery, developed postoperative chest infections and five of the eight patients who were managed with nasotracheal tubes also developed chest infections. Two of these were suspected of having aspiration pneumonitis and required tracheostomy and artificial ventilation.

There were no complications attributable to tracheostomy in any patient. One patient developed postoperative meningitis and one suffered from palatal incisional dehiscence. There were no pharyngeal wound infections.

During the 3 years, there have been five deaths, three of which occurred after discharge from hospital and from unrelated causes. There were no intra-operative deaths, but two deaths were directly attributable to surgery and anaesthesia and are described below.

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*Moffett's solution contains 2 ml 8% cocaine hydrochloride, 2 ml 1% sodium bicarbonate and 1 ml 1:1000 adrenaline.

The first patient was an 18-year-old girl with diaphyseal aclasia, who presented with spinal cord compression from atlanto-axial subluxation. Transoral decompression and posterior fusion were performed. During tightening of the interlaminar wires, complete cord compression occurred, associated with a sharp fall in blood pressure. On recovery from anaesthesia she had a dense quadriplegia and bilateral diaphragmatic paralysis. In spite of further surgical decompression, she never recovered and died 9 days postoperatively.

The second patient was a 65-year-old man with bronchial carcinoma and a metastasis in the body of the axis causing cervical cord compression, who underwent transoral anterior decompression. The following morning the nasogastric tube was inadvertently removed, he aspirated gastric contents and died of pneumonia 40 days postoperatively.

Discussion

Patients with rheumatoid disease may present difficulties at tracheal intubation.[10] This may be due to cervical spondylitis, temporomandibular joint restriction or crico-arytenoid arthritis. Five of the six patients who were difficult to intubate had rheumatoid arthritis, and one patient with advanced temporomandibular joint disease could not be intubated. We now possess a fibreoptic laryngoscope, and perform nasotracheal intubation under midazolam sedation.

The transoral route is the most direct approach to the anterior craniocervical region. However, there are particular problems relating to management of the airway. Many surgeons[3,6–8] routinely carry out tracheostomy, while others prefer the use of a tracheal tube.[9] We have used both methods.

In our early experience postoperative chest infections were more common in patients with tracheal tubes. Three of the eight patients who were initially managed with nasotracheal intubation, also eventually required tracheostomies, two due to postoperative chest infections and one due to a problem with the nasotracheal tube.

Tracheostomy allows easier observation and toilet of the pharyngeal wound, and is more comfortable for the patient. In addition, tracheostomy affords continued protection from aspiration, particularly if there is lower cranial nerve involvement or laryngeal incompetence following surgery. The earlier removal of nasotracheal tubes, as compared with tracheostomy, may in part be the reason for the increased incidence of chest infections.

We recognise that tracheostomy may be technically difficult if there is a severe flexion deformity of the neck,[10] although this problem has not arisen in these patients.

Intra-operative spinal cord damage is difficult to detect and one of the cases described illustrates its importance. Cord compression may cause hypotension (Fig. 3), but this is a relatively nonspecific indicator. Monitoring somatosensory cortical evoked potentials[9] demonstrates damage to the posterior tracts, but anterior compression is a greater hazard. It is possible that damage may be detected by changes in the respiratory pattern of spontaneously breathing patients. It is now our practice to re-establish spontaneous respiration before the interlaminar wires are tightened. Corticospinal pathway monitoring may be a better technique[11] and is currently being investigated.

Postoperative artificial ventilation was reserved for those patients who were thought to be at risk from respiratory failure. Muscle relaxants were avoided in those patients whose lungs were ventilated postoperatively since paralysis makes it difficult to assess motor power and tone. Nasogastric drainage, metoclopramide and cimetidine are essential to prevent contamination of the pharyngeal wound. Deaths from infection[3] are particularly likely in patients who are immunosuppressed from their disease or drug therapy.

Note added in proof

Since writing this review we have managed a further 20 patients by nasal intubation. Increased experience has reduced the morbidity resulting from the use of this route and it is probably the method of choice.

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Anaesthesia, 1986, Volume 41, pages 1053–1054

Compound sodium lactate (Hartmann's) solution. Caution: risk of clotting

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Summary

We have observed blood clotting in blood administration sets where Hartmann's solution (Travenol) has preceded blood transfusion. This is due to calcium ions (Ca^{++}) contained in the Hartmann's solution and is more likely to occur at 37°C. We suggest that this potential hazard be more widely realised and that the practice cease.

Key words

Complications; blood clotting.
Ions; calcium.
Transfusion; stored blood.

Hartmann's solution is frequently used as volume replacement fluid during emergency and routine surgical procedures. Last year in our district, which serves a population of 245 000, approximately 5000 litres of Hartmann's solution were used.

One of us (J.M.) has noticed that clotting occurs in the blood administration sets if blood is infused following Hartmann's solution. No instructions against this practice can be found. No adverse patient reactions have been observed in patients here, but our findings suggest that the practice be reviewed.

Methods and results

Following the observation of clotting in routine clinical practice, we repeated standard practice procedures under controlled conditions in the laboratory. Expired whole blood was passed under gravity into a blood administration set (Travenol) to which was attached a blood warmer set connected to a Fenwal blood warmer. The blood was infused at a rate of 6 ml/minute. The infusion sets were primed with standard Hartmann's solution (Travenol) and a similar isotonic solution made without calcium by our district pharmacy.

The experiment was carried out with the blood warmer switched on and with it off. Clot formation was seen in the distal drip chamber of the blood warmer set within 45 minutes of starting the blood infusion (Fig. 1.). The clots extended into the two distal loops of the warmer set. Clots were only seen when Hartmann's solution (with calcium) was used as prime with the blood warmer switched on.

In a simple mixing experiment carried out in plastic

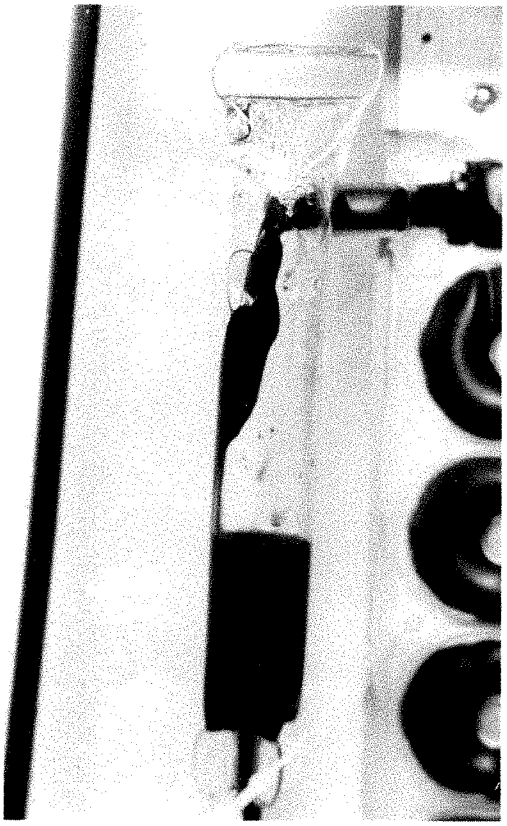

Fig. 1. Drip chamber at distal end of blood warmer set, with clot extending from entry portal.

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tubes, proportions of Hartmann's solution (H) and CPD anticoagulated blood (B) were incubated at 37°C. Ratios of H:B ranged from 1:10 to 10:1. Large clots formed within 45 minutes in the tubes with H:B ratios of 10:1 to 7:3. Calcium chloride solution in 0.9% NaCl at concentration of Ca^{++} between 0.2–4 mmol/litre were mixed with citrated blood in plastic tubes in a water bath at 37°C. Clotting was first seen within minutes at high concentration of Ca^{++} and by 45 minutes all tubes with a concentration of Ca^{++} $\geqslant 1$ mmol/litre contained clot. Calculations suggest that where a concentration of Ca^{++} $\geqslant 1$ mmol/litre exists recalcification of citrated blood occurs leading to clot formation.[1]

Discussion

The physiological formulation of Hartmann's solution has made it an attractive volume replacement fluid amongst anaesthetists and surgeons. Such balanced salt solutions have been shown to be beneficial during major surgery.[2,3] In some countries outside the UK, the problems of blood transfusion with Ca^{++} containing solutions are recognised.[4,5] Admixing blood with some other intravenous fluids has well known hazards. Dextrose solutions may damage red cells[6] and polygeline (Haemaccel) is associated with blood clotting. This gelatin solution contains 6.25 mmol/litre Ca^{++}.

It is clear that it is the Ca^{++} in Hartmann's which causes the blood to clot. Central streaming of the relatively viscous blood in the crystalloid solution results in high concentration of sodium lactate compound solution in the distal parts of the blood warmer pack. The Ca^{++} concentration exceeds the citrate's chelatable potential and clotting occurs, enhanced by the high temperature.[7]

Recent concern about microaggregates in bank blood has led to the frequent use of blood filters.[8] In the circumstances we describe, clots would form distal to any filter. We suggest that the practice of transfusion of Hartmann's type (compound sodium lactate) solutions containing Ca^{++} immediately before blood transfusion should cease. Clot formation is especially likely where a blood warmer is used in the circuit.

Acknowledgments

Our many thanks to the secretaries of the Haematology Department and Administration Department for typing the manuscript.

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Deviation from international colour codes

Accidental confusion of cylinders is a significant problem that has resulted in fatalities.[1] An international colour code has been devised and adopted in several countries, but there are countries which follow differing colour codes.[2] A different colour code system is used in Iran and a death followed accidental administration of nitrous oxide instead of oxygen.

A female patient aged 60 years in Fatai Hospital, Karadj, Iran was to have emergency surgery for a burst abdomen following extensive surgery for carcinoma of her oesophagus. The colour of oxygen and nitrous oxide cylinders is light blue in Iran, with all the markings on it in the Persian language. Anaesthesia was started by pre-oxygenation with 100 per cent oxygen for 5 minutes. The patient soon developed cyanosis and her blood pressure and pulse became unrecordable. The oxygen cylinder was checked and it was found to be nitrous oxide instead of oxygen. Immediate resuscitation was started and meanwhile a proper oxygen cylinder was attached to the Boyle's apparatus. The radial pulse returned and the systolic blood pressure was 60 mmHg but the patient did not recover consciousness and was declared dead after 4 hours.

It is astonishing that in this age of international

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standardisation there is still no mandatory standard in many countries. For the colour marking of compressed gas cylinders intended for medical use pamphlet C-9 of the Compressed Gas Association lists the cylinder colours which are recommended and followed by that particular industry. Nevertheless, the present situation is a retrogression on the earlier state and is even more confused than it was when reviewed by Hewer in 1953.[3]

The solution to the problem lies solely with the local manufacturer. Senior anaesthesiologists in university hospitals should devote their time and energy to cooperating with local manufacturers to guide them and to suggest improvements.

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Orientating under anaesthesia

This letter reports the results of two pilot studies which investigated orientating under general anaesthesia. A number of studies have sought to discover orientating responses (OR) under anaesthesia as indicators of awareness. An OR is a behavioural, or physiological, response that occurs in close temporal association to a stimulus and can be seen as a 'What is it?' response or an investigatory reflex.[1] Studies which have used ORs as evidence of awareness under general anaesthesia have included the use of EEG[2,3] and galvanic skin response (GSR).[4] Levinson found evidence of an OR to auditory stimuli under deep anaesthesia, but others[2,4] did not. It is quite likely that the salience of the stimulus (Levinson created the impression of a peri-operative crisis for the patient) is as relevant for anaesthetised patients as for normal subjects in eliciting a response. Our goal was to investigate the role of salience in GSR responses under anaesthesia.

Patients received premedication of temazepam 20–40 mg and atropine (0.6 mg) orally 1.5 hours preoperatively. Induction consisted of a sleep dose of thiopentone. Intubation was with suxamethonium 70–100 mg, followed by fentanyl 25–50 μg. Maintenance was with nitrous oxide, oxygen, halothane 1.5% or enflurane 2%. All patients were spontaneously breathing through a Bain system and had elective arthroscopies; they ranged in age from 18 to 61 years. Silver/silver-chloride nonpolarising disc electrodes were attached to the distal phalanges of the index and ring fingers.

The first pilot study endeavoured to determine whether an OR occurred to any stimulus. It is generally held that the most salient stimulus to elicit an OR is a person's name. Very few responses were made to the patient's name, or the names of the surgeon or anaesthetist. As a matter of chance we began discussing the miners' strike and found that upon mentioning Arthur Scargill, we saw a distinct response. This held true for the majority of the next dozen patients. Having found that some stimuli were more salient than others and that an OR could be observed, we constructed a more controlled study.

A 6-minute audio tape was recorded. The first 4 minutes included the names of the anaesthetist, surgeon, several two digit numbers, the sounds of Big Ben, a crowd, dogs barking, a suggestion to relax, statements that the operation was going well and that the patient would recover quickly and easily. The last 2 minutes consisted of recorded silence.

Ten patients undergoing elective arthroscopies or lateral releases participated in the study. The patient was monitored throughout the operation as in the previous study. After the patient had settled, the tape was played through headphones. The records were scored blind, using a 3 point scale of demonstrated reliability.[5] Significant differences ($p < 0.01$) were found by paired t-test, between the number of responses made while the recorded sounds were played versus the recorded silence. The number of GSR responses increased over the duration of the first 4 minutes of the tape indicated that habituation had not occurred and this cannot be invoked to account for the significant drop in the number of responses following the commencement of silence.

No GSR responses were observed to the first incision or the inflation or deflation of the tourniquet. Some time after the tape had been turned off, we noted whether responses occurred to what we felt to be particularly salient remarks made in theatre, such as details of the operation, jokes and anecdotes. We found wide individual differences. Conversation relating to the operation, either good or bad, did not necessarily elicit a response. Some jokes did, some did not, which suggests that sophisticated cognitive processing continues under general anaesthesia and, possibly, a sense of humour as well.

One question to ask is why we were able to find GSR responses when previous studies have not. We believe that the careful monitoring of the patient and the choice of salient stimuli can account for these results.

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Needle metrication

Dr M.E. Davis's suggestion (*Anaesthesia* 1986; **41:** 547–8) that the term Standard Wire Gauge should be abandoned and needle dimensions should be metricated is to be encouraged. The standard to do so is already available. Medical equipment is manufactured in accordance with a British Standard, the last of which to be produced for hypodermic needles was published in 1976,[1] when the Imperial Standard Wire Gauge designation was used. An International Standard was published in 1984,[2] which used metric measurements to designate the various dimensions. As a result, the Standard Wire Gauge is replaced by a metric equivalent as the descriptive measurement and the length is given in millimetres. Hence the 21-G hypodermic needle which is used frequently is described as 0.8 * 40.

No manufacturer seems to have replaced the old Imperial system with this metric designation, but the two designations appear together on the box and on the wrapping of needles from some manufacturers, but not all. The same standards apply also to needles used for spinal anaesthesia and with these needles the dual designation is seen more commonly, particularly for needles manufactured in Europe compared with those from the United States.

Like Dr Davis, I hope manufacturers will proceed towards metrication and compliance with the International Standard and so remove yet another potential source of confusion from medical practice.

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Nasotracheal intubation: another approach

Dr Harvey and Dr Amorosa's letter (*Anaesthesia* 1986; **41:** 442) concerning traumatic nasal intubation, prompts me to report a technique which has been designed to reduce the trauma associated with wide bore, cuffed tracheal tubes.

Sixteen adult patients scheduled for neurosurgery in the sitting position were studied. Patients were asked in the anaesthetic room to breathe through each nostril and note was taken of any difficulty; both sides were then liberally sprayed with 0.1% xylometazoline solution (Otrivine). Uncut Mallinkrodt Lo Pro tubes size 8.0 and 8.5 mm were used. The tube was lubricated with aqueous jelly and the middle finger of a large surgical glove was cut and fitted over the bevel end of the tube. Extra jelly was then applied to the protective device. Anaesthesia was induced with thiopentone 4 mg/kg and alcuronium 0.35 mg/kg. The right nostril was used in preference, unless it had been shown to be blocked. Moderate pressure was used to insert the tubes into the pharynx. If solid resisttance was encountered, the left side was tried and if this failed the procedure was abandoned. The glove finger was removed with Magill forceps under direct vision, taking care not to push it out of sight. Intubation then proceeded in the usual way, using forceps again if necessary.

Intubation was successful at the first attempt in 11 patients (69%) and in four at the second attempt (25%); there was one failure (6%). Epistaxis occurred twice (12.5%), once during a second attempt and again during the failed intubation. On two occasions small amounts of adenoidal tissue were observed on the sheath. All fifteen patients were intubated with a clean tube which showed no evidence of internal soiling.

Early reports of nasotracheal intubation stressed the importance of cocainization of the nose to produce vasoconstriction of the nasal passages. Unfortunately, a cocaine spray is no longer available in many hospitals and these results indicate that xylometazoline is a useful alternative. The use of a glove finger as a protective sheath serves two functions. Firstly, it protects the nasal passages from the hard edges of the tube bevel, so that the tube is an obturator rather than a curette. Secondly, the cuff is protected from the nasal conchae. Used in combination, nasotracheal intubation may be accomplished with minimal trauma to the nasal passages. Some practice is required before confidence is gained by the operator and in this respect I am indebted to my anaesthetic colleagues at the Ulster Hospital, Belfast, who taught me this method with skill and patience.

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Psoas compartment block

Odoom *et al.* (*Anaesthesia* 1986; **41:** 155–8) state that psoas compartment block may be used to achieve complete analgesia of the lower extremity. They also recommend its use for hip surgery. We disagree with both these points: complete analgesia of the lower limb can only be achieved by separate sciatic nerve block, combined with a psoas compartment block.[1] Chayen *et al.* state that a sciatic nerve block should be added if the procedure includes the posterior thigh or lower limb.[1] We would suggest that this also includes hip surgery, because part of the nerve supply comes from the sciatic nerve. Psoas compartment block alone is not adequate for hip surgery, because the skin over the area of the incision is supplied by the twelfth thoracic nerve. This nerve does not pass through the psoas compartment.

We have been using the combined psoas compartment and sciatic nerve block for leg surgery for 10 years. It is our preferred method of anaesthesia and we use it routinely unless the patient prefers a general anaesthetic. Our technique is as follows. The patient is seen pre-operatively, the procedure is explained and their consent obtained. Premedication is with lorazepam 2.5 mg to the average patient, 2 hours pre-operatively. An intravenous infusion is set up. The patient's blood pressure and ECG are monitored. He is placed in a lateral decubitus position, with the side to be operated uppermost. The landmarks are identified and marked. We use the technique described by Winnie *et al.* to locate the lumbar plexus[2] and that of Labat to locate the sciatic nerve;[3] 23-gauge needles are then used with a nerve stimulator set at 2 Hz to locate the nerves. Careful aspiration for blood and cerebrospinal fluid precedes injection of 30–40 ml of 1% mepivacaine with 1:600,000 adrenaline to block the lumbar plexus and 15–20 ml for the sciatic nerve.

We use mepivacaine because it has medium duration of action, usually between 3 and 3.5 hours for surgery and a further 3 hours for postoperative analgesia. However, we have had blocks lasting up to 17 hours. Mepivacaine causes less vasodilatation than other agents and hypotension has never occurred. Mepivacaine provides excellent motor blockade, which bupivacaine 0.25% does not and it is also less toxic. No toxic reaction to this dose of mepivacaine has occurred in over 2000 cases. General anaesthesia is not used since it is not necessary, but sedation is sometimes required during prolonged cases. We consider that bupivacaine is not the drug of choice because of the large dose required and because the duration of action (876 minutes in Odoom's paper) is much longer than is necessary.

The combined lumbar plexus and sciatic nerve block is a very useful technique for analgesia of the lower limb. It avoids the hazards of spinal or epidural and it blocks only the leg to be operated on. Once the technique is mastered it only takes about 10 minutes to perform and the block is complete after 20 minutes.

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A reply

Thank you for giving us the opportunity to respond to the letter from Drs Barrett and Mostarlic.

The aim of the study presented in our article was to determine the plasma concentration of bupivacaine after the large volumes of either plain bupivacaine 0.25% or bupivacaine 0.25% with adrenaline (1:200 000) which are needed to fill the psoas compartment for an adequate block. We recommended 40 ml of 0.25% bupivacaine with adrenaline (1:200 000) for hip surgery since our study demonstrated that it was safe. It was not our primary intention to assess the adequacy of this form of locoregional analgesia for hip surgery. This has been demonstrated by other authors.[1]

We cannot agree with Drs Barrett and Mostarlic that sciatic nerve block is either necessary or desirable for hip surgery. This type of surgery involves regions which are not supplied by either the sciatic nerve or the T_{12} nerve as suggested by them. In our opinion, block of the sciatic nerve is superfluous and causes discomfort to the awake patient.

Radiographic studies in patients carried out by us (unpublished data) have demonstrated a successful psoas compartment block for hip surgery with a complete imaging of the psoas muscle.[1] It is therefore likely that the iliohypogastric nerve may be blocked in the psoas compartment. The iliohypogastric nerve contains sensory and motor fibres from T_{12} and L_1, pierces the greater psoas muscle and leaves to innervate the anterosuperior region of the iliac spine.

We regularly use psoas compartment block alone without general anaesthesia in approximately 30% of patients presenting for hip surgery. However, in the remaining patients we supplement this with light general anaesthesia for three reasons: patients want to be asleep, (particularly the elderly patients) light general anaesthesia is preferable to sedation and a clear airway can be guaranteed.

In our department, the average duration of this type of surgery is 2–3 hours and this is uncomfortable for the patient (semiprone with the unaffected extremity flexed at the knee and hip).

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Premedication for children

Recent correspondence makes it plain that there is no consensus on the premedication of children. This is even more true of children admitted for day-case procedures; indeed, one review paper stated that a suitable premedicating drug for premedication of children is badly needed.[1]

We have a weekly afternoon operating session in which between 10 and 18 children undergo anaesthesia for minor ENT operations; the majority of these children are day-cases. Trimeprazine (3–4 mg/kg) is unsuitable for these children, since up to 50% of them are too sleepy to be discharged the same afternoon. We have not found that papaveretum and hyoscine produces the total absence of crying or struggling found by Carter[2]; we consider that no premedication can do this.

We decided to try the suggestion of Fry,[3] that very small doses of trimeprazine were suitable as premedication for children. Our initial impression was that this was indeed the ideal. There was none of the uncooperative drunkenness often seen with more sedative drugs and almost all the children showed no distress either before or during induction of anaesthesia. Indeed, microdose trimeprazine became part of our standard technique, taught to several annual cohorts of trainees.

We have now undertaken a randomised double blind trial of this against placebo. A group of 101 children aged 1–12 years, scheduled for surgery, were premedicated with either trimeprazine syrup (6 mg) ml; Vallergan Forte, May & Baker Ltd) or a similar inert syrup. Children aged 2–4 years received 1 ml of syrup and 0.25 mg oral atropine; those aged 5–8 years old received 1.5 ml and those 9–12 years old, 2 ml of syrup (both without atropine). Anaesthesia was induced with thiopentone, cyclopropane or halothane. The two groups were similar in age, weight and emotional state.

Table 1. Comparison of children on arrival in the anaesthetic room; asleep, drowsy or calm was considered satisfactory, anxious or crying, unsatisfactory.

	Placebo	Trimeprazine
Satisfactory	43	31
Unsatisfactory	8	19
χ^2	4.51; $p < 0.05$	

Table 1, shows that the placebo is superior. All children were able to go home the same day and many had already left hospital by the end of the operating list.

This study confirms that small doses of trimeprazine can cause arousal,[4] which appeared as anxiety. We cannot recommend the use of this dose of trimeprazine as a premedication for children; at present we use no premedication, with excellent effect. The vital aspect of pre-operative preparation for these patients is sympathy and kindness; the children are not confined to bed and are allowed to continue playing until the time for the operation arrives.

Any study of premedication in children should include a placebo as one of the alternatives.

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Difficult extubation due to a kinked pilot tube

We recently had difficulty at extubation when the pilot tube of a Mallinckrodt tracheal tube was kinked by the retaining bandage and the cuff failed to deflate. The Mallinckrodt Lo-Pro tube is described as for oral or nasal use. These combined plastic tubes have a higher take-off point for the pilot tube than red rubber Magill, or oral-use only, plastic tubes (Table 1). This incident would not have occurred if the take-off point of the pilot tube had been lower down.

Table 1. Characteristics of some of the tubes available at this hospital

Tube type (size 8)	Manufacturer's description	Distance to take-off point of pilot tube (cm)
Red rubber Magill	oral	13.5
Franklin Clearway	oral	18.5
Mallinckrodt Lo-Pro	oral/nasal	20.5
Shiley low pressure	oral/nasal	20.5

We suggest that manufacturers should consider replacing the take-off point to the previous lower position. This would also overcome the difficulty which occurs when a tracheal tube is cut to an appropriate length for a short-necked patient, if the take-off point is high.

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Kinking of epidural catheters

We have read with interest the article by Drs Kumar, Dennison and Lawler (*Anaesthesia* 1985; **40:** 1100–2). This prompts us to report our experience with a single hole epidural catheter made of rilsan, a material which is said to have advantages for this application because it is not only stronger but easier to insert than the existing epidural catheter. Of the first thirty catheters apparently uneventfully inserted into the lumbar epidural space for pain relief in labour, seven were found to be blocked on initial injection of local anaesthetic solution. In some cases, withdrawal of the catheter 1 or 2 cm relieved this obstruction, but the remaining catheters had to be removed. On removal, the catheters were found to be kinked at varying points proximal to the tip, thus completely occluding the catheter lumen. While the blockage problem was normally immediately obvious, on one occasion the catheter became occluded after three successful top-up doses had been given and on close examination of the catheter the kinking was found to be outside the epidural space.

This experience raises a number of points about the design of epidural catheters and their insertion. Single end-hole catheters (such as the rilsan catheter used above) need not be advanced more than 2 cm into the epidural space. Further advancement only increases the risk of catheter kinking and displacement. Should any resistance to catheter insertion be encountered at any time, this might indicate a real risk of catheter kinking. Our experience shows that subsequent occlusion may be relieved by withdrawing the catheter slightly. Obviously it pays to check catheter patency both before inserting a catheter and before the securing dressing is applied. Certain needles are said to have been designed to facilitate catheter insertions through peri-needles and these make it easier to apply excessive force during such insertion. With floppy catheters this may increase the risk of catheters kinking whilst with stiffer catheters there may be more risk of dural puncture from the catheter. Excessive resistance to catheter insertion should be treated with due respect and the epidural repeated if necessary.

The most commonly used catheter in our department is that made by Portex (three lateral eyes in a closed end; ref no. 100/382/116) and the majority of users leave at least 3 cm of the catheter in the epidural space which is in accordance with the advice of Drs Kumar, Dennison and Lawler.

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A reply

It is interesting to hear of the experiences of Drs Gough, Johnston and Harmer with regard to the kinking of several epidural catheters. We agree that single-end-hole catheters need to be advanced only 2 cm, or indeed less, into the epidural space. The advantages of floppy catheters would appear to be marginal, since any claimed benefits may be outweighed by the risk of kinking.

Perhaps the optimal catheter design with presently available materials, is a stiff single end-hole catheter (Portex Ref. No. 100/382/216). The end hole permits minimal distance of insertion and this, together with the stiffer design, should minimise the problem of kinking.

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B. DENNISON
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Rusty water in an oxygen flowmeter

A recent incident at our hospital serves to emphasise the hazards of incorrect storage of cylinders. A 7-month-old girl presented with stridor, shortness of breath and recurrent chest infections. Chest Xray showed that her trachea was markedly displaced anteriorly and rather narrowed. Ultrasound showed a fluid-filled cyst in the mediastinum and a scan was requested.

She was anaesthetised in the paediatric theatre anaesthetic room, her trachea was intubated and lungs ventilated via a Mapleson E system from an oxygen cylinder. On arrival at the scan room, after uneventful transport, it was noticed that some rust-coloured fluid suddenly filled the flowmeter on the oxygen cylinder, pushed the bobbin upwards and entered the fresh gas tubing. The breathing system was changed rapidly to that on the anaesthetic machine in the scan room. No fluid or rusty material was detected at the patient end of the line and indeed no change was noted in the patient, who was being monitored by a precordial stethoscope. The scan proceeded uneventfully and operation for removal of a large unilocular bronchogenic cyst was undertaken the following week. The patient has done well postoperatively, with no evidence of stridor but she is still susceptible to chest infections.

What was the material in the flowmeter and tubing? Our technicians examined the tubing and found it to be rusty water. The cylinder was sent to the British Oxygen Company (BOC) who dismantled it. Their report stated that the inside of the cylinder was quite dry with no evidence of water having entered it. There was, however, a film of rust which had formed around the threads of the valve. The conclusion drawn by BOC was that the cylinder must have been left outside without a protective cap and that water was not removed from the valve outlet when the regulator was connected. They assured the department that all their cylinders undergo rigorous checking and that the gas is of correct standard for medical use; however, they warned that if cylinders need to be stored in the open then the cap should be replaced and the cylinder stored on its side to eliminate water from the valve.

It would seem appropriate to reiterate that cylinders need to be stored correctly to prevent this alarming occurrence happening again. It was fortunate that the patient appears to have suffered no harm.

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D.J. SCHILLER

Lumbar sympathetic block in the sitting position

Two recent publications on chemical lumbar sympathectomy seem to indicate increasing interest in this procedure, which has something to offer to those among the increasing number of the elderly who suffer from peripheral vascular disease.[1,2] There is a simple modification of the conventional technique which we find has several advantages.

Lumbar sympathetic block is usually done either with the patient prone or lying on the unaffected side. Both positions have their disadvantages. Some elderly patients, even when sedated, find it distressing to lie prone for any length of time, or to keep still in the lateral position. Recently, analogous to spinal and epidural techniques, we have done blocks in the sitting position. The patient sits across the table, leaning on screen supports fixed parallel to the edge. An intravenous infusion is set up and the blood pressure, electrocardiogram and skin temperature are monitored.

We find that patients tolerate the position better and no sedation is needed. It helps open up the space between the lower ribs and the iliac crest; also, it is much easier to judge the orientation of the needle and to manipulate the image intensifier. A radiolucent table is not necessary and since gas-filled bowel is not squeezed into the upper abdomen as in the prone position, and one is imaging through the patient only, the picture is clear. Gravity aids the downward spread of the phenol solution and possibly achieves more widespread destruction of the sympathetic chain.

We use the landmarks described by Hughes-Davies and Redman.[3] We aim for the second lumbar ganglion and inject 1 ml meglumine iothalamate (Conray 280) to define the tissue plane before injecting 10 ml 7.5% aqueous phenol solution. So far we have injected five patients in the sitting position. The indication in each case was severe rest pain and complete relief has occurred in all patients. This may not be unusual, but we are impressed by the ease of the method for us and the lack of distress for the patients.

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Pain on injection with propofol

We wish to comment on the problem of pain on injection of propofol. In their paper, McCulloch and Lees (*Anaesthesia* 1985; **40:** 1117–20) found 37% of patients complained of pain when propofol was injected into the veins on the dorsum of the hand. This high incidence was not reduced significantly by pretreatment with lignocaine.

This is in agreement with our finding[1] of a 50% overall incidence of pain on injection of propofol into the dorsal hand veins, which we were unable to diminish by premedication, or by giving both fentanyl and lignocaine before propofol. We then added lignocaine to the propofol emulsion and, after obtaining the approval of the Committee for the Safety of Medicines, we found that use of this mixture reduced the incidence of pain to 4%.

In a subsequent investigation, again using the propofol and lignocaine mixture,[2] we found an overall incidence of pain on injection of 3.7%. These results were significantly better than those obtained by pretreatment with lignocaine[1] and allow propofol to compare more favourably with thiopentone with respect to pain on injection.

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A reply

Pain on injection with propofol is a major drawback of a potentially extremely useful drug. The mixing of lignocaine with propofol as described by Dr Brooker and Dr Redfern would appear to lower the incidence of pain on injection with this drug. However, mixing lignocaine and propofol does raise the possibility of an undesirable pharmacological reaction as described by Gibb, but is well worth further investigation.

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Dilution of alfentanil in clinical practice

In their article (*Anaesthesia* 1985; **40:** 298–9) Dr Wright and colleagues highlighted the possible risk associated with the dilution of anaesthetic agents. They point out that commercially available preparations of drugs used in anaesthesia may be of a concentration inappropriate for immediate use. In some circumstances, this could lead to potentially dangerous situations.

Clinical experience with alfentanil in patients who are expected to breathe spontaneously has shown that this very short-acting narcotic is best used in small, repeat bolus doses. It is clear that many anaesthetists dilute the current formulation, (Rapifen 0.5 mg/ml) in clinical practice. To avoid the problems associated with inaccurate dilution a dilute formulation of alfentanil (Rapifen Paediatric 0.1 mg/ml) has been introduced.

We expect that anaesthetists may find this new formulation particularly appropriate for use with children and elderly patients. Experience suggests that spontaneous ventilation is more easily maintained when alfentanil is injected slowly, a task made easier with this new presentation. In order to avoid confusion we have deliberately introduced the new concentration of alfentanil in a different size of ampoule.

In summary, the three formulations of alfentanil are identified by brand name, ampoule size, pack markings and ampoule markings. Details and further information are available from the Anaesthetists Information Service at this address.

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Children and explosive anaesthetics

We frequently use cyclopropane for induction of anaesthesia in this hospital. Its use is restricted to the anaesthetic room and it is only administered by an open system (the end of the anaesthetic tubing is held in the hand close to the patient's face). We have had no unfortunate occurrences with cyclopropane and consider it a useful induction agent for children.

However, cyclopropane is explosive and comments made by colleagues at recent anaesthetic meetings have caused us some concern; some people have expressed surprise that cyclopropane is being used at all in 1986. We are told that not all paediatric hospitals use cyclopropane, implying that we may be in the minority; it has even been suggested that should an explosion occur and the patient be injured, any claim for damages would be indefensible.

Two recent reports of explosions in the operating theatre remind us we cannot afford to be complacent in this matter.[1,2] The theatre environment must be kept inherently safe by properly maintained antistatic precautions and care with the positioning of other possible sources of ignition. However, we wonder how many hospitals actually do check their floors, shoes, and anaesthetic systems every 6 months as recommended,[3,4] and how many anaesthetists have noticed the increasing number of electrical devices appearing in theatres with warning notices against their use near flammable anaesthetic agents.

We feel it would be unfortunate not only for the patient, but also for anaesthesia as a whole if cyclopropane came into disrepute due to accidents caused by improper use, but maybe we are in the minority. We would therefore welcome comment, especially from other children's centres, on the use of cyclopropane. Are we out on a limb, or are we part of generally acceptable practice?

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Antistatic precautions

We are in the process of laying down the specifications for our new hospital theatres and we are scrutinising every aspect of the design for its cost benefits. One apparent anachronism has appeared. We have not used any explosive anaesthetic agents for the last 10 years and so have saved ourselves a small fortune by removing the need for maintenance of antistatic precautions; this has also allowed us to introduce equipment into the theatre that does not meet explosion-proof standards.

Nevertheless, we are having pressure put upon us to have our new theatres built to antistatic standards, since this is 'Departmental Policy'; the DHSS is, apparently, ready to accept advice from the profession on this subject. My proposal is that explosive agents should, in future, be used only in *specially* equipped theatres.

It is an unnecessary extravagance to build and maintain every theatre to antistatic standards and indeed our present policy is dangerous since many theatres that at first sight appear to meet these standards, have not had proper checks or maintenance for many years. Thus, anaesthetists may be lulled into a false sense of security.

Such a change of policy would still allow the use of explosive agents by those who wish to do so, but nevertheless produce considerable savings to the NHS at trivial inconvenience to the profession, and no compromise of standards for patient care.

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All that wheezes is not asthma—again

The account of possible red rubber sensitivity (*Anaesthesia* 1986; **41:** 549–50) in which bronchospasm arose in an asthmatic patient 20 minutes into the anaesthetic, suggests to me an alternative explanation. The musical quality of wheeze is attributed to the reed-like mechanism at a narrowing in a tube; this induces resonance in the column of gas within it. Thus, partial obstruction of the lumen of a tracheal tube at its tip by cuff herniation may mimic bronchospasm.

The parodoxical ausculatory features, lack of response to bronchodilator therapy yet immediate resolution on substituting another (admittedly not red rubber) tracheal tube described by Basavaraja *et al.* are exactly those of intermittent obstruction of the tracheal portion of the airway. Whereas some constituents of rubber products are potential allergens, established asthma does not remit in 20 seconds.

Significant changes in cuff pressure are known during a nitrous oxide anaesthetic. A well-used red rubber tube may have an excessively compliant cuff and thus, after 20 minutes, may have increased in volume sufficiently to herniate over the tip of the tube and present significant obstruction. Asthmatics do have a more labile bronchomotor tone and indeed, bolus administration of histamine-releasing anaesthetic agents tends to produce bronchospasm at induction.

The occurrence of 'bronchospasm' in the middle of an anaesthetic should always raise the suspicion of a mechanical problem such as obstruction of the tube or pneumothorax, particularly if there are no features of histamine release such as cutaneous flushing or if drugs or blood have not been administered, for halothane and enflurane are both potent bronchodilators.

Finally, the use of aminophylline in the presence of hypoxia is particularly liable to induce ventricular dysrhythmias. If bronchospasm does arise in the middle of an anaesthetic, cuff herniation can be diagnosed and cured simultaneously by deflation of the pilot balloon before reaching for the aminophylline.

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Another complication of central venous catheterisation

We would like to report an unusual complication of central venous catheterisation. A 26-year-old male presented for a right preumonectomy for a destroyed tuberculous lung. A 70-cm central venous catheter was placed via the left basilic vein. It appeared to be swinging and giving reasonable readings.

The surgeon had to remove part of the azygos vein, but when the vein was divided, 2 cm of the tip of the central venous catheter was found in the dissected portion. The proximal part of the catheter was embedded in the ligated azygos stump, which had to be loosened and then re-tied once the catheter was withdrawn. The rest of the operation proceeded uneventfully.

This mishap was of little importance in this case, but there is obviously potential for catastrophic haemorrhage if a catheter is overlooked.

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Armoured tubes are necessary for neuroanaesthesia

Dr Wright (*Anaesthesia* 1986; **41:** 213) stated in his recent letter that use of an armoured tracheal tube for neuroanaesthesia does not appear to be justified. However, as many have before us, we have encountered kinking of an ordinary disposable tube during neurosurgical operations, in two instances over the past 13 months. We describe here the details of those cases.

A 62-year-old woman with a right parietal metastasis from a cancer of the lung, underwent a 9-hour craniotomy for removal of the tumour. Anaesthesia was induced with thiopentone 250 mg intravenously and an 8.5 mm cuffed Portex disposable tracheal tube was inserted with the aid of 100 mg of suxamethonium. Anaesthesia was then maintained with nitrous oxide, oxygen and enflurane. She was placed in the prone position with head flexed. Ventilation was manually assisted throughout the operation, with intermittent intravenous injection of 10–40 mg of suxamethonium for relaxation. Anaesthesia was uneventful. At the end of operation, while she was still in the prone position, manual compression of the reservoir bag suggested partial respiratory obstruction. Therefore, a 14 FG Portex curved tipped suction catheter was introduced into the tracheal tube, but could not be passed the full length of the tube. An X ray of the head and neck was immediately taken and revealed kinking of the tracheal tube in the pharynx (Fig. 1). Meanwhile, the operation was concluded, the patient was placed supine and the tracheal tube removed. Her postoperative course was uneventful.

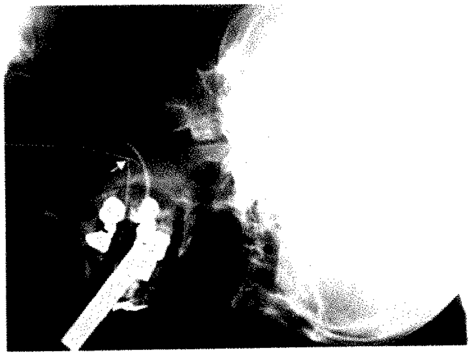

Fig. 1. Arrow indicates kinked portion of the tracheal tube.

A 26-year-old woman with a left parietal meningioma underwent a 9-hour craniotomy for removal of the tumour. Anaesthesia was induced with thiopentone 300 mg intravenously and an 8.5 mm Portex disposable tracheal tube was introduced with the aid of 100 mg of suxamethonium. Anaesthesia and ventilation were then maintained as before. She was placed in the left lateral decubitus, with head flexed and rotated to the right. Ten minutes before the end of the operation, we found that the 14FG Portex curved

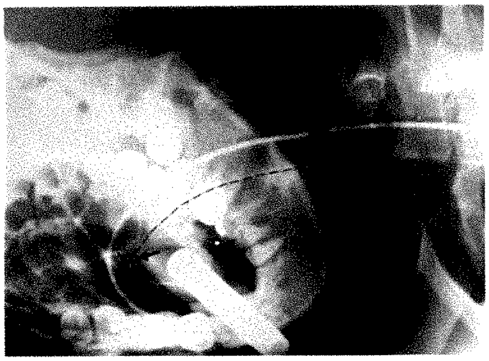

Fig. 2. Arrow indicates kinked portion of the tracheal tube.

tipped suction catheter could not be passed through the tube due to kinking of the tube (Fig. 2). Flexion and rotation of her head were corrected and she was placed supine. Thereafter, selective left and right bronchial suctioning[1] was possible and the trachea was extubated. Her postoperative course was uneventful.

Arai and Kuzume[2] reported three instances of kinking of Portex blue-line tracheal tubes during neurosurgical operations in which flexion of the neck was minimal. They claimed that kinking occurred because of a structural fault in the tube. In both of our cases, it was fortunate that kinking of the tube occurred at the end of the operation. However, kinking of the tube might occur at any time in a patient with the head flexed, with disastrous results. We have therefore abandoned the use of cuffed Portex disposable tracheal tubes for neurosurgical operations in which the head must be flexed and we have been using Aire-Cuf (Bivona Inc.) armoured tracheal tubes without any airway trouble. However, even an armoured tracheal tube does not guarantee the patency of the airway, for various reasons; nevertheless, we consider the armoured tubes to be safer than the ordinary disposable tube. The most important factors in early detection of airway obstruction include close observation, manual ventilation of the lungs to test compliance and selective bronchial suctioning during anaesthesia.[1] In order to prevent coughing as the trachea is suctioned during craniotomy, temporary paralysis with suxamethonium is used.

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The collator of this section is Dr L. Laufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data is held on Dbase II, and is available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

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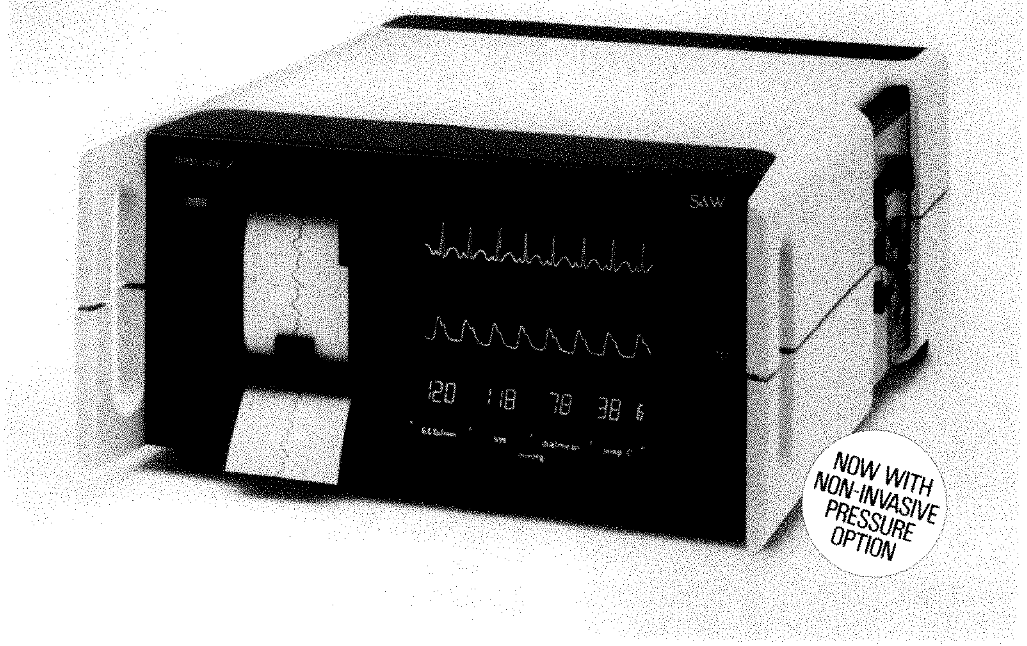
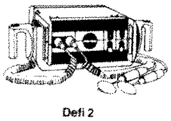
S&W

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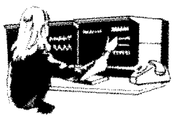
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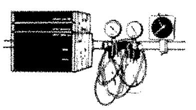
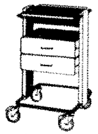
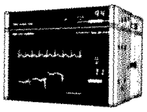

Modura Rail
The original "Danish Rail" system


Medicart
Multipurpose trolleys designed especially for medical use.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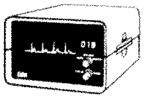
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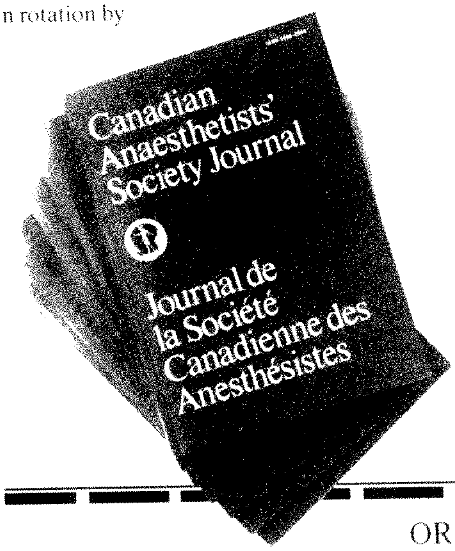
Each journal issue contains a Continuing Medical Education Section provided in rotation by Canadian university Departments of Anaesthesia. The CME section summarizes clinically relevant information intended for all anaesthetic practitioners.

The Annual Meeting Supplement produced as Part II of each May issue contains Refresher Course Outlines and abstracts of papers presented in the Scientific Programme of the Annual Meeting of the Canadian Anaesthetists' Society held in June of each year.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Anaesthesia, 1986, Volume 41, pages 1073–1081

News and notices

Stop Press. *Readers of this section are also referred to the Stop Press page at the end of this section.*

Obituaries

Hardman, Una Margaret (née Campbell), FFARCS. Formerly anaesthetist of the Neurological Unit, Royal Sheffield Infirmary. Qualified from University of Leeds in 1939.

Hicks, Dorothy Myrtle, FFARCS. Consultant anaesthetist United Leeds Hospitals. Qualified from University of Leeds in 1940.

Kay, Robert Stewart, FFARCS. Formerly consultant anaesthetist to the East Suffolk and Ipswich Hospital. Qualified from the University of Glasgow in 1930.

Roper, Richard Edward, FFARCS. Consultant anaesthetist at Whiston Hospital. Qualified from the University of Liverpool in 1968.

Wynne, Robert Llewellyn, FFARCS. Formerly anaesthetist at Birkenhead General and Wallasey Central Hospital. Qualified from University of Liverpool in 1927.

Association of Anaesthetists of Great Britain and Ireland

The Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA, England. Telephone: 01–631 1650 (Ansafone service available out of office hours).

Standing notices

Full details of the activities of the Association are published in the January edition of *Anaesthesia* (106–111). These include details of membership publications of the Association, educational and historical information.

Future meetings of the Association

Annual Scientific Meetings

1987—Sheffield, 10–11 September.
1988—Southampton, 15–16 September.

Linkman Conferences

1987—Sheffield, 9 September.
1988—Southampton, 14 September.

Competence to practise

The Association of Anaesthetists of Great Britain and Ireland and the Royal College of Psychiatrists are cooperating in a scheme to help sick anaesthetists early in their illness.

The system depends upon voluntary reporting by colleagues and is not coercive. It must be emphasised that this scheme is supplementary to existing controls. Fitness to practise may be impaired through illness and the sick doctor for various reasons may not take any steps to remedy the situation. The scheme provides machinery whereby confidential psychiatric help can be offered to the ailing doctor from a source outside his own Region.

The reporting clinician should contact the office of the Association of Anaesthetists to ascertain the name of a referee (Dr P.J. Helliwell, Dr D.C. Howat, Dr S.A. Mason) and need not identify himself to the office staff. The reporting clinician will be given the name, telephone number and availability of the referee. Preferably, a second clinician will also be required to confirm the report to the referee. The referee will then contact a psychiatrist from another Region nominated by the College of Psychiatrists from a prepared list: the psychiatrist will then get in touch with the potential patient.

No further information will be transmitted through the system unless the potential patient does not accept the offer of a visit to the nominated psychiatrist. In that case, the reporting physician(s) will be informed after a month that treatment has not been accepted.

Suitable arrangements have been made for confidential treatment of the doctor-patient in another Region and for the reimbursement of travel expenses.

EEC Monospecialist Committee for Anaesthesia

Guidelines for the facilities required for the administration of day-to-day routine anaesthesia

Copies of the above document setting out the
recommended facilities and equipment
administration of routine (non special
are available from the Association's off
prove helpful as an *aide memoire* to thos
developments involving the specialty.

The Junior Anaesthetists' Group of the Association of Ana of Great Britain and Ireland

All junior members of the Association are members of the Group. The Group committee has representation on various committees of the Association and Faculty.

Chairman: Dr G.W. Hamlin (*Leeds*).
Honorary Secretary: Dr L. Allan (*Pentland Grove House, Seafield by Roslin, Midlothian, Edinburgh EH25 9RQ. Tel. (031) 445 2313.*

Future meetings

1987—Belfast, 8–10 April (Junior Linkman Meeting, April 7).
1988—Nottingham, 5–8 April.

The Junior Anaesthetists' Annual Prize

This is a competition held at the An
Meeting of the Junior Anaesthetists G
8–10 April 1987) and consists of ten-
which are presented by junior member
session of the meeting. The rules for th
were published in *Anaesthesia* 1982; **37:**
The closing date for submission of ab
competition is 1 February, 1987, an
abstracts should be forwarded by then t
tion offices.

Faculty of Anaesthetists of the Royal College of Surgeons o

The Faculty of Anaesthetists of the Royal College of Surgeons of England, 35–43 Lincoln's Inn
WC2A 3PN. Telephone: 01–405 3474

Faculty News

Birthday Honours

The Dean and Board of Faculty offer their congratulation to Dr J.E. Riding who was awarded the CBE in the recent Birthday Honours.

Election of President and Vice-Presidents

The Dean and Board of Faculty congratulate Mr I. Todd on his election as President, Professor D. Campbell on his election as Senior Vice President, and Mr P. Lord on his election as Junior Vice President of the Royal College of Surgeons of England.

Examination results

At the Part 3 FFARCS examination he
94 of the 372 candidates were successf
At the Part 2 FFARCS Examinatio
1986, 119 of the 267 candidates were
At the Part 2 FFARCS Examination
in April/May, 1986, 5 of the 9 c
successful.
At the Part 1 FFARCS Examinati
1986, 200 of the 398 candidates were
At the Part 1 FFARCS Examination
in April/May, 1986, 9 of the 21 c
successful.
At the Part 1 FFARCS Examination
in May, 1986, 5 of the 12 candidates

Faculty of Anaesthetists of the Royal College of Surgeons

The Faculty of Anaesthetists of the Royal College of Surgeons in Ireland, 123 St Stephen's Gre
Telephone: Dublin 780200 (Ext 268).

Dean: Dr P.W. Keane.
Vice-Dean: Dr D.C. Moriarty.

Honorary Secretary: Dr D.F. Hogan.
Honorary Treasurer: Dr J.C. Cooper.

Educational activities

Postgraduate course

Part II, FFARCSI, Course, 13–17 October 1986.

Lectures

Inaugural lecture, 6 November 1986, Professor A.J. Cunningham, Royal College of Surgeons in Ireland, Dublin.

Winter Faculty Lecture, 12 December 1986. Dr L. Saidman (*USA*).

Annual Scientific Meeting of the Faculty, 15–16 May 1987.

Section of Anaesthetics of the Royal Society of Medicine

Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE. Telephone: 01–580 2070

President: Dr W.D.A. Smith OBE.
Secretaries: Dr G.M.C. Patterson (*Nuffield Department of Anaesthetics, The Radcliffe Infirmary, Oxford OX2 6HE*). Professor T.E.J. Healy. (*Manchester*).

Meetings of the Section are held on the first Friday in the month, beginning in November, and are held at 1 Wimpole Street, London W1M 8AE, at 5.30 p.m.

Fellows of the RSM are welcome to bring guests if they wish.

Programme

1986

7 November—*Presidential Address: Sense and insensibility.*
5 December—*Is anaesthesia bad for us?—aspects of occupational health.*

1987

9 January—*Work in progress: Applications of spinal anaesthesia.*
6 February—*Symposium on legal aspects of anaesthesia.*
6 March—*Practice makes perfect?—Studies on repeat anaesthetics.*
3 April—*Anaesthesia and surgery for congenital craniofacial abnormalities.*
8 May—*May & Baker RSM Prizes. AGM. Annual Dinner.*
5 June—*All-day symposium: Medical emergencies.*
2 October—*Sir Robert Macintosh's 90th Birthday, (17 October 1987) a tribute. Followed by a reception given jointly with the Association of Anaesthetists of Great Britain and Ireland and the Faculty of Anaesthetists of the Royal College of Surgeons of England.*

Specialist Societies

British Association for Immediate Care (BASIC)

Chairman: K.C. Easton, OBE.
Secretary: Hamish McLeod (*The Hope, Moffat Dumfrieshire. Tel: Moffat 20314*).

Society of Anaesthetists of the British Forces in Germany

President: Professor J.P. Payne (London).
Secretary: Major S.T. Inglis, FFARCS, RAMC (BMH Rinteln, BFPO 20 Germany).

Association of Cardiothoracic Anaesthetists

Honorary Secretary: Dr R.D. Latimer (*Papworth Hospital, Papworth Everard, Cambridge CB3 8RE. Tel: 0480 830541*).

Future meetings

1986—12 December, Royal Society of Medicine, London.
Information: Dr R. Feneck (*London Chest*) *Hospital, Bonner Road, London E2 9JX*).

1987—26 June, Cambridge.
Information: Dr I. Hardy (*Papworth Hospital, Papworth Everard, Cambridge CB3 8RE*).
Autumn Meeting, Liverpool.
Information: Dr J.C. Richardson (*Broadgreen Hospital, Thomas Drive, Liverpool L14 3IB*).

1988—Spring Meeting, Cambridge.
Information: Dr J. Kneeshaw, (*Papworth Hospital, Papworth Everard, Cambridge CB3 8RE*).

Association of Dental Anaesthetists

President: Dr T.M. Young (*Manchester*).
Secretary: Dr M.A. Skivington (*Department of Anaesthetics, Poole General Hospital, Poole, Dorset BH15 2JB*).
Assistant Secretary/Editor: Dr M.E. Ward (*Oxford*).

Future Meetings

1987—17 January, Guy's Hospital, London. (Please note change of venue).
Information: Dr R.M. Jones.

11 July. Plymouth.
Information: Dr F.S. Keddie.
1988—1–4 June. Guernsey.

History of Anaesthesia Society

President: Dr J.A. Lee (*Southend-on-Sea*).
Vice-President: Dr T.B. Boulton (*Oxford and Reading*).
Honorary Treasurer: Dr A. Padfield (*Sheffield*).
Honorary Secretary: Dr I. McLellan (*Department of Anaesthesia, Groby Road Hospital, Leicester LE3 9QE*).

Inaugural Meeting

The Society was inaugurated at a meeting at the Royal Berkshire Hospital, Reading, on 7 June 1986.

Membership

Membership is open to all those interested in the history of anaesthesia, whether medically qualified or not.

Future meeting

1987—7 February, St Bartholomew's Hospital, London. The host will be Dr D. Wilkinson. Free papers are invited.
Information: Dr D. Wilkinson, St Bartholomew's Hospital, London EC1A 7BE.

Intensive Care Society

Chairman: Dr S.M. Willatts (*Bristol*).
Meetings Secretary: Dr C.J. Hinds (*St Bartholomew's Hospital*).
Secretary/Treasurer: Dr D. Ryan (*Intensive Therapy Unit, Freeman Hospital, Newcastle upon Tyne NE7 7BE*).

Future meetings

1986—1 November, Hospital for Sick Children, London.
1987—9–11 April. Exeter University.

The Intractable Pain Society of Great Britain and Ireland

Chairman: Dr K. Budd (*Bradford*).
Honorary Secreatry: Dr T.P. Nash (*Basingstoke District Hospital, Aldermaston Road, Basingstoke, Hampshire RG24 9NA*).

Prize Essay

An annual competition is held for the best essays related to pain relief. Submissions to the Honorary Secreatry by 31 August 1987. Essay contents are judged in two groups. Doctors in training and Society members.

Future Meetings

1987—9–11 April, Annual General Meeting and Scientific Meeting, Liverpool.
Hosts: Drs C. Wells and S. Lipton.
5–6 June, Behavioural treatments in chronic pain. A celebration of 150th anniversary of St Andrew's Hospital, Northampton.
Host: Dr K. Trick.

Neuroanaesthetists' Travelling Club

Information: Dr S.B. Foulds, Salford Health Authority, Peel House, Albert Street, Eccles, Manchester M30 0NJ.

Obstetric Anaesthetists' Association

President: Dr D.D. Moir (*Glasgow*).
Honorary Secretary: Dr J. Thorburn (*Department of Anaesthesia, The Queen Mother's Hospital, Yorkhill, Glasgow G3 8SH*).
Treasurer: Dr A.P. Rubin (*London*).
Minute Secretary: Dr B.R. Wilkey (*Cambridge*).
All UK membership enquiries to Dr J. Thorburn, please.

Association of Paediatric Anaesthetists

President: Dr G.W. Black (*Belfast*).
Honorary Secretary: Dr P. Morris (*Royal Manchester Children's Hospital, Pendlebury, Manchester M27 1HA*).

Future meetings

1987—20–21 March. Leeds.
Information: the Honorary Secretary.
5–6 June, Paris. Joint meeting with the French Society of Paediatric Anaesthetists.
Information: the Honorary Secretary.
12–13 June, Great Ormond Street, London. Seminar on Paediatric anaesthesia.
Information: Dr D.J. Hatch, Department of Anaesthesia, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JH.

Plastic Surgery and Burns Anaesthetists

President: Dr C.C.M. Howie (*Bangour*).
Honorary Secretary: Dr F.J.M. Walters (*Department of Anaesthetics, Frenchay Hospital, Bristol BS16 1LE*).

Enquiries about membership to the Honorary Secretary, please.

The Russell Davies and Stuart Laird Prize

The Society wishes to announce that this prize, £200, has been generously donated by Abbott Ltd. The prize will be awarded for an essay connected with anaesthesia and plastic and burns surgery and is open to any career anaesthetist in the National Health Service. Further details are obtainable from the Honorary Secretary.

Anaesthetic Research Society

Chairman: Professor A.A. Spence.
Honorary Secretary: Dr A.R. Aitkenhead (*University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW*).

Future Meetings (closing dates for papers)

1986—15 November (3 October). St Bartholomew's Hospital, London.
1987—20 March (6 February). University of Oxford.
26–27 June (8 May) University of Glasgow.
13–14 November (25 September) Northwick Park Hospital.

Special Notice

Abstracts are photoreduced and must be submitted on a preprinted form, which is available from the Hon. Secretary. All correspondence and abstracts should be sent to the Hon. Secretary.

Resuscitation Council (UK)

Chairman: Mr A. Marsden.
Secretary: Dr D.A. Zideman (*Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS*).

Advanced Life Support

Posters which illustrate the Council's recommendations for Advanced Life support are now available.

Home news and notices

Scottish Society of Anaesthetists

President: Dr A.I. MacKenzie, (*Carluke*).
Vice-President: Dr W.R. Macrae, (*Edinburgh*).
Honorary Secretary: Dr W.F.D. Hamilton, (*Department of Anaesthesia, Ninewells Hospital, Dundee DD1 9SY*).
Honorary Treasurer: Dr I.G. Gray (*Dundee*).

National and local events

October 1986

3 *FFARCS Part 1/DA(UK)* Applications due.

3 *Clinical Trials in Anaesthesia:* Kelvin Conference Centre, Glasgow.
Information: Secretary, University Department of Anaesthesia, Glasgow Royal Infirmary, 8–16 Alexandra Parade Glasgow G31 2ER.

3 *North of England Society of Anaesthetists.* Presidents Night: Dr F.B. Buckley.
Information: Dr J.E. Charlton, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP.
Yorkshire Society of Anaesthetists. Title to be announced.
Information: Dr J.S. Gibson, Leeds General Infirmary, Leeds LS1 3EX.

7–9 *FFA Part 1/DA (UK) Course*, Birmingham.
Information: Postgraduate Secretary, PGMC, East Birmingham Hospital B9 5ST.

8 *Yorkshire Society of Anaesthetists.* Dr T.S. West, Terminal Care and the Control of Pain.
Information: Dr J.S. Gibson, Leeds General Infirmary, Leeds LS1 3EX.

8 *Northern Ireland Society of Anaesthetists.* Dr R.M. Jones, Perioperative Cardiac Dysrhythmias.
Information: Dr J.E. Hegarty, Department of Anaesthetics, 97 Lisburn Road, Belfast BT9 7BL.

9–10 *Anaesthesia symposium.* (Janssen Pharmaceuticals) York. Aspects of recovery from anaesthesia.
Information: Dr I. Hindmarch, Human Psycho-Pharmacology Unit, University of Leeds (Tel: 0532–44607).

8–15 *FFARCS (Ireland).* Revision Course: Part 2.
Information: Honorary Secretary, Faculty of Anaesthetists, Royal College of Surgeons in Ireland, St Stephen's Green, Dublin 2.

13 *Wessex Anaesthetic Club.* Dr H.T. Davenport, Anaesthesia in the Elderly.
Information: Dr D.V. Rutter, Southampton General Hospital, Southampton SO9 4XY.

14 *Reading Anaesthetists.* Title to be announced.
Information: Dr A.M. Barr, Royal Berkshire Hospital, Reading, Berks RG1 5AN.

16 *Manchester Medical Society.* Section of Anaesthetics. Presidential Address: Dr C.B. Franklin, Anaesthesia from the Elbe to the Oder.
Information: Dr E.E.M. Thompson, University of Manchester, Oxford Road M13 9PL.

17 *FFARCS (Ireland) Part 1* begins

17 *FFARCS (Ireland) Part 3.* Applications due.

18 *Postgraduate Study Day* jointly organised by the Faculty and the Association.

20 *FFARCS Part 2.* Vivas begin.

22 *Whole Day Symposium.* Respiratory Problems in Anaesthesia, Coventry.
Information: Dr C.J. Knickenberg, Department of Anaesthetics, Walsgrave Hospital, Coventry CV2 2DX. Tel: 613232 ext 580.

24 *FFARCS (Ireland) Part 2* begins.

24 *Liverpool Society of Anaesthetists.* Prof. W.S. Nimmo. Variability of Drug Response in Anaesthesia.
Information: Dr A.M. Florence, Broadgreen Hospital, Liverpool L14 3LB.

November 1986

1 *Intensive Care Society* at Hospital for Sick Children, London.
Information: Dr C.J. Hinds, St Bartholomews Hospital, London EC1A 7BE.

4 *Royal College of Pathologists.* Symposium on Pathology of Trauma. Robin Brook Centre, St Bartholomew's Hospital, London.
Information: Scientific Meetings Officer, Royal College of Pathologists, 2 Carlton House Terrace, London SW1Y 5AF.

5 *Northern Ireland Society of Anaesthetists.* Prof. I. McA. Ledingham. The Role of Intensive Care in Modern Medicine.
Information: Dr J.E. Hegarty, Department of Anaesthetics, 97 Lisburn Road, Belfast BT9 7BL.

6–7 *Faculty Symposium, London.* Safer Obstetric Anaesthesia.
Information: Mr S.N. Alan, Secretary, Faculty of Anaesthetists, Royal College of Surgeons, 35/43 Lincolns Inn Fields, London WC2A 3PN.

7 *Section of Anaesthetics Royal Society of Medicine.* Dr W.D.A. Smith, Presidential Address, Sense and insensibility.
Information: Sections Office RSM 1, Wimpole Street, London W1M 8AE.

7 *North of England Society of Anaesthetists.* Title to be announced.
Information: Dr J.E. Charlton, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP.

8 *N.E. Thames Regional Society of Anaesthetists.* Meeting at University College Hospital.
Information: Dr J.D. Hill, St Margarets Hospital, Epping, Essex CM16 6TN.

11 *Reading Anaesthetists,* Dr J.N. Lunn. *Mortality and anaesthesia.*
Information: Dr A.M. Barr, Royal Berkshire Hospital, Reading, Berks RG1 5AN.

12 *Yorkshire Society of Anaesthetists.* Prof. G. Jones. An Aspect of Depth of Anaesthesia.
Information: Dr J.S. Gibson, Leeds General Infirmary, Leeds LS1 3EX.

14 *FFARCS Part 1/DA (UK):* Written Papers.

15 *Anaesthetic Research Society.* St Bartholomew's Hospital, London.
Information: Dr A.R. Aitkenhead, Leicester Royal Infirmary, Leicester LE1 5WW.

15 *Society of Anaesthetists of Wales.* Annual Dinner, Seabank Hotel, Porthcawl.
Information: Dr R. Mason, Morriston Hospital, Swansea SA6 6NL.

16 *Manchester Medical Society, Section of Anaesthetics.* Dr P.J.F. Baskett, Aspects of Resuscitation.
Information: Dr E.E.M. Thompson, University of Manchester, Oxford Road M13 9PL.

21 *Scottish Society of Anaesthetists.* Annual Scientific Meeting and Gillies Memorial Lecture at Kelvin Conference Centre, Glasgow.
Information: Dr W.F.D. Hamilton, Dept. of Anaesthesia, Ninewells Hospital, Dundee DD2 1UB.

26 *Northern Ireland Society of Anaesthetists.* Dr A.K. Adams. Reflections of an Anaesthetist.
Information: Dr J.E. Hegarty, Department of Anaesthetics, 97 Lisburn Road, Belfast BT9 7BL.

28 *FFARCS Part 3.* Applications due.

28 *East Midlands Intensive Care Travelling Club* at Rotherham.
Information: Dr V. Boyd, Rotherham District General Hospital, Rotherham S60 2UD.

December 1986

1 *Wessex Anaesthetic Club.*
Information: Dr D.V. Rutter, Southampton General Hospital SO9 4XY.

2 *Edinburgh & East of Scotland Society of Anaesthetists.*
Information: Dr D.G. Littlewood, Royal Infirmary, Edinburgh EH3 9YW.

3 *Northern Ireland Society of Anaesthetists.*
Information: Dr J.E. Hegarty, Queens University, 97 Lisburn Road, Belfast B9 7BL.

3 *Bristol Anaesthetic Club.*
Information: Dr P. Thornton, Bristol Maternity Hospital, Southwell Street, Bristol BS2 8EG.

4 *Liverpool Society of Anaesthetists.* Dr J.F. Nunn, Free Radicals and Oxygen Toxicity.
Information: Dr A. Florence, Broadgreen Hospital, Liverpool L14 3LB.

5 *North of England Society of Anaesthetists.* Title to be announced.
Information: Dr J.E. Charlton, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP

5 *Section of Anaesthetics, Royal Society of Medicine.* Is anaesthesia bad for us?—Aspects of occupational health.
Information: Sections Office RSM 1, Wimpole Street, London W1M 8AE.

8 *Wessex Anaesthetic Club.* Prof. Alex Paton, The Journal Mountain.
Information: Dr D.V. Rutter, Southampton General Hospital, SO9 4XY.

9 *Reading Anaesthetists.* Title to be announced.
Information: Dr A.M. Barr, Royal Berkshire Hospital, Reading, Berks RG1 5AN.

10 *Yorkshire Society of Anaesthetists.* Title to be announced.
Information: Dr J.S. Gibson, Leeds General Infirmary, Leeds LS1 3EX.

11 *Manchester Medical Society Section of Anaesthetics.* Title to be announced.
Information: Dr E.E.M. Thompson, University of Manchester, Oxford Road M13 9PL.

12 *Irish Faculty.* Winter Lecture.

12 *Association of Cardiothoracic Anaesthetists* at the Royal Society of Medicine.
Information: Dr R. Feneck, London Chest Hospital, Bonner Road, London E2 9JX.

15 *FFA Part I/DA (UK) London.* Vivas begin.

International news

The Society of Anaesthetists of Hong Kong

President: Dr J. Allison (*Nethersole Hospital*).
Honorary Secretary: Dr T.W. Lee (*Prince of Wales Hospital*).

Summary of President's Report for 1986

Nine scientific meetings were held and one meeting in combination with the Critical Care Society. Two meetings were locally arranged symposia. An explanatory document for patients was circulated. The Board of Anaesthesia and Intensive Care was formed to plan for future developments in Hong Kong.

The Society intends to follow up the Kwangzhou Society's suggestion of combined meetings with their Society.

International congress calendar

1986

1–3 October. Alexandria. *Autumn meeting of Egyptian Anesthesiologists.*
Information: Dr M.H. Shaker, PO Box 71, Dokki, Giza, Egypt.

3–5 October. Mombasa. *Annual Scientific Meeting Society of Anaesthesiol. of East Africa.*
Information: Dr P.O. Huma, PO Box 20819, Nairobi, Kenya.

10–11 October. Manila. *'October Affair' Philippine Society of Anesthesiologists Inc.*
Information: Dr N.D. Santos, Medical Ass. Building, North Avenue, Diliman, Quezon City, Philippines.

17–21 October. Las Vegas. *Annual Meeting American Society of Anesthesiologists.*
Information: J.W. Andes, Esq., 515 Busse Highway, Park Ridge, Illinois 60068, USA.

18–21 October. Perth, Western Australia. *Annual Meeting of the Australasian Society of Anaesthetists.*
Information: Secretariat ASA, PO Box 345, Paddington, NSW 2021, Australia.

18 October. Seoul. *31st Annual Congress Korean Society of Anesthesiologists.*
Information: Dr Choi Byung-Kwon, Room 607, Teh Korean Medical Ass. Building, Seoul 140–00, Korea.

19–22 October. Santiago. *XIV Congreso de Anestes de Chile.*
Information: Dr S. Barros Recabal, Hospital de Coya, Servicio de Anestes. 'El Teniente'. A. Republica de Chile 592, Rancagua, Chile.

23–25 October. Oslo. *Annual Meeting and General Assembly Norsk Anestesiologisk Forening.*
Information: Dr Svein Sunde, Anestesiavd, Ullevaal Sykenhus, 0407 Ullevaal, Oslo, Norway.

23 October. Prague. *National meeting Czech Society of Anaes. and Resuscitation.*
Information: Dr J. Drabkova, c/o Professor J. Pocta, Inst. of Anaesth and Resus. Srobarova 50, 100 34 Praha 10, Vinobrady, Czechoslovakia.

23–25 October. Lugano. *Annual Meeting SGAR and SGI.*
Information: Dr D. Bernhardt, B. Rudt, Gutenbergstr. 3 3011 Bern, Switzerland.

25 October. Paris. *Mises au point en anesthesie-reanimation.*
Information: M.A.P.A.R Bicetre, Departement d'Anesthesie-Reanimation, CHU de Bicetre, 78 Reu du General-Leclerc, 94275 Le Kremlin-Bicetre Cedex, France.

31 October–2 November. Bogota. *2nd Course on Pain.*
Information: Dr A. Leon D, Transv. 5 49-00 Piso 13, Hospital Militar, Apartado Aereo 11206, Bogota, Colombia.

31 October–1 November. Santiago de Cuba. *II National Symposium Sociedad Cubana de Anestesia y Reanimacion.*
Information: Dr J. Santos Gracia, Calle 4 No. 407, Entre 19 y 17 Vedado, Habana 4, Cuba.

31 October–4 November. Buenos Aires. *XVIII Jornadas*

Argentinas de Anestesiologia.
Information: Dr E. Weissbrod, Aranguren 1323, (1405) Buenos Aires, Argentina.

6–8 November. Helsinki. *Annual Meeting Finnish Society of Anaes.*
Information: Dr L. Kaukinen, Inkerink 14, SF 33730 Tampere 73, Finland.

13–16 November. Halifax, Nova Scotia. *Canadian Anaesthetists' Society Atlantic Meeting.*
Information: Mr Lloyd H. Mayeda, 94 Cumberland Street, Suite 901, Toronto, Ontario, Canada M5R 1AS.

20–21 November. Poprad. *National meeting Czech Society of Anaes.*
Information: Professor J. Pocta, Inst. of Anaes. & Resusc. Srobarova 50, 100 34 Praha 10, Vinobrady, Czechoslovakia.

24–29 November. Kiev. *11 International Symposium of Anaesthesiologists of the Socialist Countries.*
Information: Organising Committee, Dept. of Anaesthesia, Bakulev Inst. of Cardiovascular Surgery, Leninsky Prospect 8, Moscow, USSR.

27–30 November. Grenoble. *4th International Conference on Disaster Medicine.*
Information: Ste Intern, Medecine de Catastrophe, PO Box 59, 1213, Petit Lancy 2, France.

29 November. Brussels. *Stutory General Assembly Societe Belge d'Anest et de Reanimation.*
Information: Professor P. de Temmerman, Chaussee de Namur 1, B 3045 Blanden, Belgium.

30 November–4 December. Erevan. *Society of Anaesthesiol. of Armenia, USSR.*
Information: Dept. of Anaesthesia, Bakulev Inst. of Cardiovascular Surgery, Leninsky Prospect 8, Moscow, USSR.

10–11 December. Manila. *Yuletide Symposium Philippines Society of Anesthesiologists, Inc.*
Information: Dr. N.D. Santos, Medical Ass. Building, North Avenue, Diliman, Quezon City, Philippines.

1987

12–15 January. Berlin. *10 National Congress 'Anaesthesia '87'.*
Information: Dr Pickart, Karowerstr. 11, DDR-1115 Berlin-Buch, GDR.

31 January–7 February. Vail, Colorado. *12th Annual Vail Conference in Anesthesiology.*
Information: Professional Seminars, PO Box 012318, Miami, Florida 33101, USA.

8–12 February. Sheraton Waikiki Hotel, Waikiki, Hawaii. *15th Obstetric Anesthesia Conference.*
Information: The Ohio State University Hospital, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210.

8–12 March. Kiandra Lodge, Vail, Colorado. *7th Medical Monitoring Technology Conference.*
Information: The Ohio State University Hospital, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210.

14–18 March. Florida, USA. *61st Congress of the International Anesthesia Research Society.*
Information: E.A. Moffitt, Executive Secretary, International Anesthesia Research Society, 3645 Warrensville Center Road, Cleveland, Ohio 44122.

15–19 March. Bloemfontein, *South African Society of Anaesthetists.*
Information: The Chairman, 1987 SASA Congress, Department of Anaesthesiology (G67), Faculty of Medicine, PO Box 339, Bloemfontein 9300, South Africa.

22–27 March. The Lodge at Vail, Vail, Colorado. *14th Neonatal and Infant Respiratory Symposium.*
Information: The Ohio State University Hospital, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210.

2–4 April. Tokyo. *34th Annual Meeting Japan Society of Anesthesiologists.*
Information: Dr K. Mori, 5F, TY Building, 18-11 Hongo 3-chome, Bunkyo-ku, Tokyo.

7–9 May. Paris. *VI Annual Meeting of the European Society of Regional Anaesthesia.*
Information: M.A.P.A.R, Departement d'Anesthesiologie, Hopital de Bicetre, 94270 Kremlin-Bicetre, France.

28–31 May. Chanea, Crete. *7th Congress of the Greek Society of Anaesthesiologists.*
Information: Greek Society of Anaesthesiologists, 34 Dragoumi Street, 115 28 Athens, Greece.

13–18 June. Calgary, Alberta. *Canadian Anaesthetists' Society Annual Meeting.*
Information: Mr Lloyd H. Mayeda, 94 Cumberland Street, Suite 901, Toronto, Ontario, Canada M5R 1AS.

20–25 June. Montreal, Canada. *XIII International Symposium on Cerebral Blood Flow and Metabolism.*
Information: Sorelcomm (1985) Inc., Conference Secretariat, 1425 Dorchester Boulevard West, Montreal, Canada H3G 1T2.

29 June–3 July. Linkoping. *19th Scandinavian Congress.*
Information: Dept. of Anaesthesiology, University Hospital, S-581 Linkoping, Sweden.

2–7 August. Hamburg. *Vth World Congress on Pain.*
Information: Hamburg Messe & Congress, Postfach 30 24 80, 2000 Hamburg 36, FRG.

23–28 August. Sydney, Australia. *10th International Congress of Pharmacology.*
Information: The Secretariat, 10th IUPHAR Congress, GPO Box 2609, Sydney, NSW 2001, Australia.

2–5 September. Singapore. *5th ASEAN Congress of Anaesthesiologists.*
Information: World Express PTE Ltd, 114 Meddle Road 01-01, Singapore 0718.

10–11 September. Sheffield. *Annual Scientific Meeting*

Association of Anaesthetists of Great Britain and Ireland.
Information: The Honorary Secretary, 9 Bedford Square, London WC1B 3RA.

15–18 September. Paris. *IIIrd International Symposium on Pediatric, Surgical and Neonatal Intensive Care.*
Information: S.O.C.F.I., 14 Rue Mandar, 75002 Paris, France.

10–14 October. Atlanta. *Annual Meeting American Society of Anesthesiologists.*
Information: J. Andes, Esq., 515 Busse Highway, Park Ridge, Illinois 60068, USA.

1988

22–28 May. Washington, D.C. *9th World Congress of Anaesthesiology.*
Information: American Soc. of Anaesthesiologists, 515 Busse Highway, Park Ridge, Illinois 60068, USA.

15–16 September. Southampton. *Annual Scientific Meeting, Association of Anaesthetists of Great Britain and Ireland.*
Information: The Honorary Secretary, 9 Bedford Square, London WC1B 3RA.

18–21 October. Perth. *Annual General Meeting Australian Society of Anaesthetists.*
Information: The Secretariat, ASA, PO Box 345, Paddington, New South Wales 2021, Australia.

Anaesthesia, 1986, Volume 41, page 1082

Safety Information Bulletin

These are issued by the Department of Health and Social Security

Treonic C30 Infusion Controller

These have been supplied in the past by Vickers Medical but are now marketed by Travenol Laboratories Limited. There are three particular problems associated with their use.

1. It is important that the drop chamber be not tilted.
2. Some controllers do not establish and maintain control at infrequent drop rates, particularly below 9 drops/minute.
3. The clamp mechanism within the controller does not always completely close the tube.

The latter two points require that the apparatus should be checked and if necessary the supplier of the particular C30 should be contacted.

Lung ventilator, Blease Manley Model MP3

The piston and seals of the expiratory tap assembly should be replaced annually. The plastic piston within this gradually becomes brittle with time and with regular autoclaving.

Breathing system conical fittings (SIB (86) 39)

Pre-assembled components have become mis-shapen or assemblies have fallen apart and do not make a satisfactory joint when re-assembled. Individual components may distort if placed under other items. Both these effects have followed autoclaving and users are recommended to process plastic conical fittings, which are claimed to be re-usable, only in accordance with the manufacturers' recommendations. Single-use items should not be re-sterilised or re-used.

Syringe pumps: Vickers Treonic IP4 and IP5 series

A splashproof cover should be fitted to the flow selector switch of these models. Pumps with serial numbers greater than 118 002497 also have a switch-monitoring circuit. Models with lower serial numbers can be modified.

Enquiries about all the above may be made to the appropriate person as specified below.

England
Mr R.A. Page,
DHSS,
Scientific and
Technical Branch,
14 Russell Square,
London WC1B 5EP
(Tel. 01 636 6811 Ext. 3259)

Wales
Dr J.A.V. Pritchard,
Scientific Adviser,
Welsh Office,
Cathays Park,
Cardiff CF1 3NQ
(Tel. 0222 823912)

Scotland
Scottish Health Service,
CSA, Supplies division,
Scientific and
Technical Branch,
Trinity Park House,
South Trinity Road,
Edinburgh EH5 3SH
(Tel. 031 552 6255
Ext. 2478)

N. Ireland
Chief Engineer's Branch,
Department of Health
and Social Services,
Central Works Unit,
Stoney Road,
Dundonald,
Belfast BT16 0US
(Tel. Dundonald 4535
Ext. 28)

Anaesthesia, 1986, Volume 41, page 1083

Errata

Anaesthesia, 1986, Volume 41, page 670

Overdose of intrathecal morphine

In this letter from Dr Pomonis, 0.015 grams of morphine were given and not 0.15 grams as stated. Furthermore, the names of two further authors of the letter, G. Economacos and S. P. G. Costopanajiocoy, were accidentally omitted.

Anaesthesia, 1986, Volume 41, pages 703–707

Nitrous oxide anaesthesia and vomiting

D. S. LONIE AND N. J. N. HARPER

The sentence beginning on line 17 of the Patients and methods section (p. 703) should read: In group A, anaesthesia was maintained with nitrous oxide 67 percent in oxygen and 1.25 minimum alveolar concentration (MAC) . . .

Anaesthesia, 1986, Volume 41, page 1084

Stop press

1988

22–28 May. Washington D.C. *9th World Congress of Anaesthesiology*

Information: American Society of Anesthesiologists, 515 Busse Highway, Park Ridge, Illinois 60068, U.S A.

THIS PAGE CONCERNS YOU IF YOU ARE A MEDICALLY QUALIFIED ANAESTHETIST IN GREAT BRITAIN AND IRELAND, OVERSEAS OR IN TRAINING AND ARE NOT YET A MEMBER OF THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND OR IF YOU ARE A MEMBER OF ANOTHER PROFESSION WHO PRACTISES IN ANAESTHESIA AND YOU WISH TO APPLY FOR ASSOCIATE MEMBERSHIP

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The Association of Anaesthetists of Great Britain and Ireland
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London WC1B 3RA, England

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........................19

To the Honorary Secretary,
Association of Anaesthetists of Great Britain and Ireland

I (full name).. offer my name as a candidate
BLOCK LETTERS

for (a) MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) JUNIOR MEMBERSHIP of the Association (*please delete categories not applicable*)*

I hold the following appointment(s) as an anaesthetist (*please state grade if in the National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia*):

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....

....

Qualifications (with dates)..

....

(Signed)..

Address..
....Hospital Tel. No:......................................
....Home Tel. No:...

We, being Members† of the Association, nominate as a candidate for MEMBERSHIP/OVERSEAS/ASSOCIATE/JUNIOR MEMBERSHIP

....

1. (Signed)..
(NAME IN BLOCK LETTERS)
Address..
BLOCK LETTERS

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(NAME IN BLOCK LETTERS)
Address..
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* See the reverse of this page for details of membership categories.
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Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Articles accepted become copyright of *Anaesthesia*.

Contributors are requested to submit two copies of manuscripts. They are also advised to retain a third copy as the Editors cannot accept responsibility for the loss of manuscripts in the post. The covering letter should be signed personally by all the authors and careful consideration should be given to the decision to include more than five authors. Articles should be forwarded to:

*Dr J. N. Lunn, Editor of **Anaesthesia**, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.*

PREPARATION OF MANUSCRIPTS

Articles for *Anaesthesia* should be prepared in accordance with *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5) except that the titles of journals in the reference section should be given in full (see below). A reprint of these requirements of which this notice is a summary, can be obtained from the *British Medical Journal* price 50 pence (U.K.).

Type manuscripts on white bond paper, 20.3 × 26.7 cm or 21.6 × 27.9 cm (8 × 10½ in. or 8½ × 11 in.) or ISO A4 (212 × 297 mm) with margins of at least 2.5 cm (1 in.). Use double, and preferably triple, spacing throughout, including the references. Please do not use a dot matrix printer, particularly one with poor quality descenders or ascenders. Unseparated, fan-folded manuscripts may be returned to the author.

The manuscript should consist of the following sections in this order each beginning on a new page: *title page*, *summary* and *key words*, *text*, *acknowledgments*, *references*, *individual tables*, and *legends for figures*.

Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page.

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The name of the author and the address to which proofs and other correspondence is to be addressed should appear in the top left-hand corner of the sheet.

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Start a new sheet

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Key (indexing) words. Below the abstract, provide and identify as such, three to 10 key words or short phrases that will assist indexers. Use terms from the Medical Subject Headings list from *Index Medicus*. The Editor may modify these at proof stage to conform with agreed practice of certain other anaesthetic journals in the English language.

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(*continued overleaf*)

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The text of observational and experimental articles, case reports, etc. is usually divided into sections with the headings *Introduction, Methods, Results* and *Discussion*. Long articles will need subheadings within some sections to clarify their content.

Letters for the correspondence pages should be double spaced and prepared in accordance with the format in a recent copy of *Anaesthesia*.

Headings: three steps of heading may be used in typescripts:

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(ii) Underlined words

These should be typed at the left hand side of the page above the paragraph which they precede.

(iii) Underlined words at the beginning of a paragraph. These may either be followed by a full stop or form part of the first sentence of the paragraph.

ACKNOWLEDGMENTS

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Acknowledge those who have made substantive contributions to the study or the preparation of the manuscript. Authors are responsible for obtaining written permission for publication of reproduced figures and tables from authors and publishers and from everyone acknowledged by name because of copyright conventions and because readers may infer their endorsement of the data and conclusions.

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Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by arabic numerals. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. Use double or treble space typing.

Use the form of reference adopted by the U.S. National Library of Medicine and used in *Index Medicus*. Use the style of the examples cited at the end of this section.

The titles of journals should be given in full.

Avoid using abstracts as references except those published in a recognised journal. 'Unpublished observations' and 'personal communications' may not be used as references, although references to written, not verbal, communications may be inserted (in parentheses) in the text. Include among the references manuscripts accepted but not yet published; designate the journal followed by (*in press*) in parentheses. Information from manuscript submitted but not yet accepted should be cited in the text as (unpublished observations) in parentheses.

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Examples of correct form of references

Note: first and last pages in all references.

JOURNAL

Standard journal article—(List all authors)

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294:** 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

Osler AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

Rhodes AJ, Van Rooyen CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences.* 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

Weinstein L, Swartz MN Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: WB Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, Md: National Center for Health Statistics, 1972. (*Vital and health statistics. Series* **10:** Data drom the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

Do not include tables in the text. Start a new sheet for each table and space the material adequately. The author(s) name(s) should appear in the top right-hand corner.

Indicate the approximate position of each table in relation to the subject matter of the text in the right-hand margin of the appropriate page on the manuscript. Do not submit tables as photographs. Number tables consecutively with arabic numerals. Supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all non-standard abbreviations that are used in each table. For footnotes, use the following symbols in this sequence: *, †, ‡, §, ||, ¶, **, ††, etc. Identify statistical measures of variations such as SD and SEM. *Legends for tables* should appear on the face of the table.

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Start a new sheet

Type legends for illustrations double spaced with arabic numerals corresponding to the illustrations. When symbols, arrows, numbers or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

CONVENTIONS AND ABBREVIATIONS

Statistics and measurements should be given in figures except that numerals one to nine should be in words if not followed by a measurement symbol (e.g. 'two patients' but '2.0 mg'). The *Système International* (SI) will usually be used except that vascular pressures will be recorded in mmHg and cmH_2O. Imperial measurements will not be used except in an historic context. The 24 hour clock will be used.

Contributors are advised to study the SI *Conversion Tables* provided in the January 1978 issue of *Anaesthesia, Units, Symbols and Abbreviations* (*A Guide for Biological and Medical Editors and Authors*) published by the Royal Society of Medicine, London W1M 8AE, and *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5).

LETTERS FOR PUBLICATION

Should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University of Wales Hospital, Heath Park, Cardiff CF4 4XW, UK.

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The editors regret that failure to comply with the above requirements may result in a delay in publication of accepted papers.

REVIEW JOURNALS

This journal is covered by *Current Contents, ASCA* and the *Science Citation Index*.

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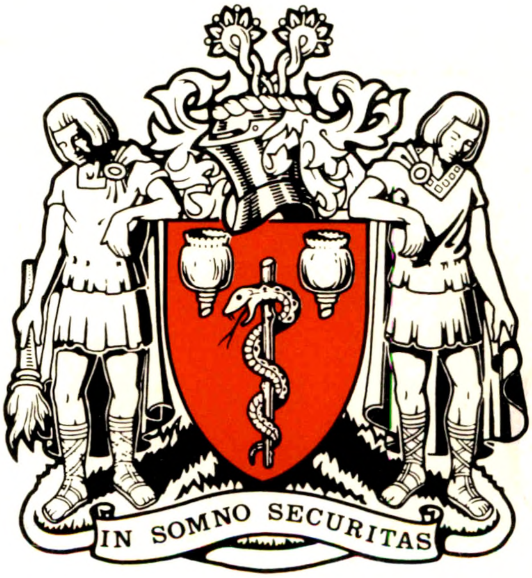
Anaesthesia

Journal of the Association of Anaesthetists of Great Britain & Ireland

Volume 41 Number 11 November 1986



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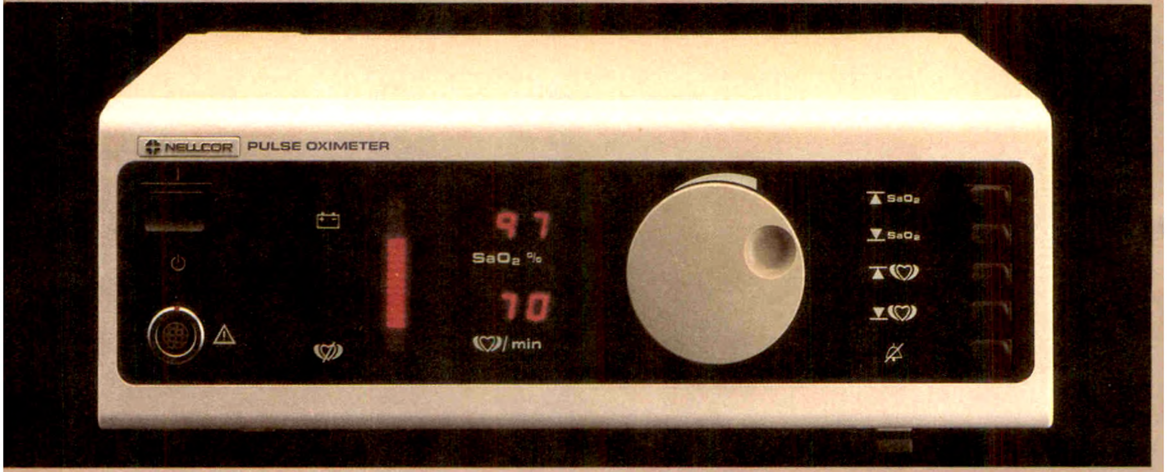

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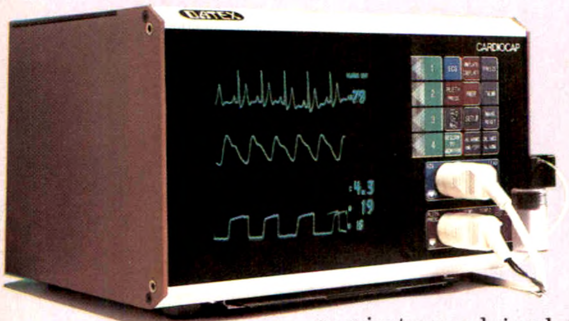

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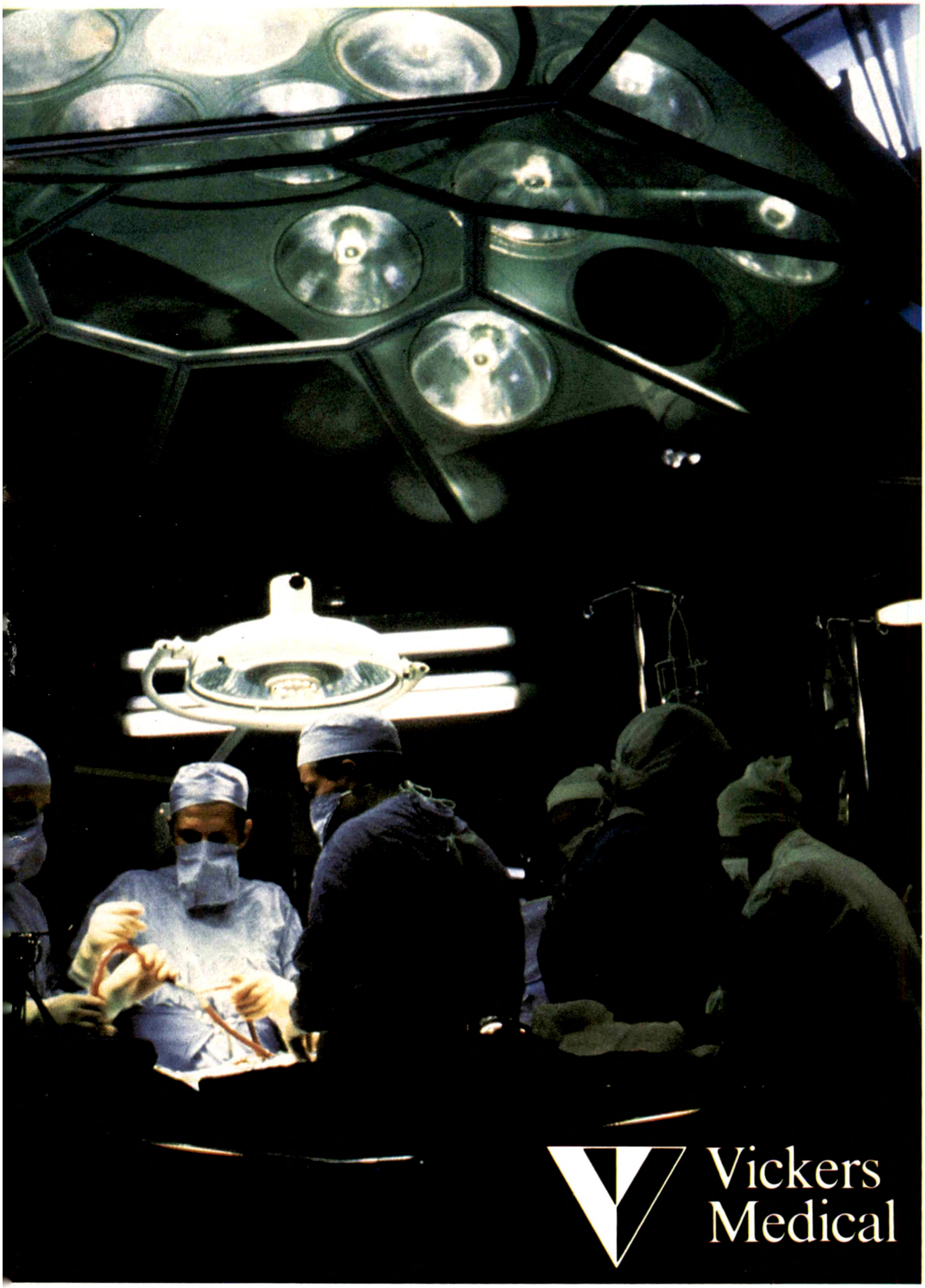

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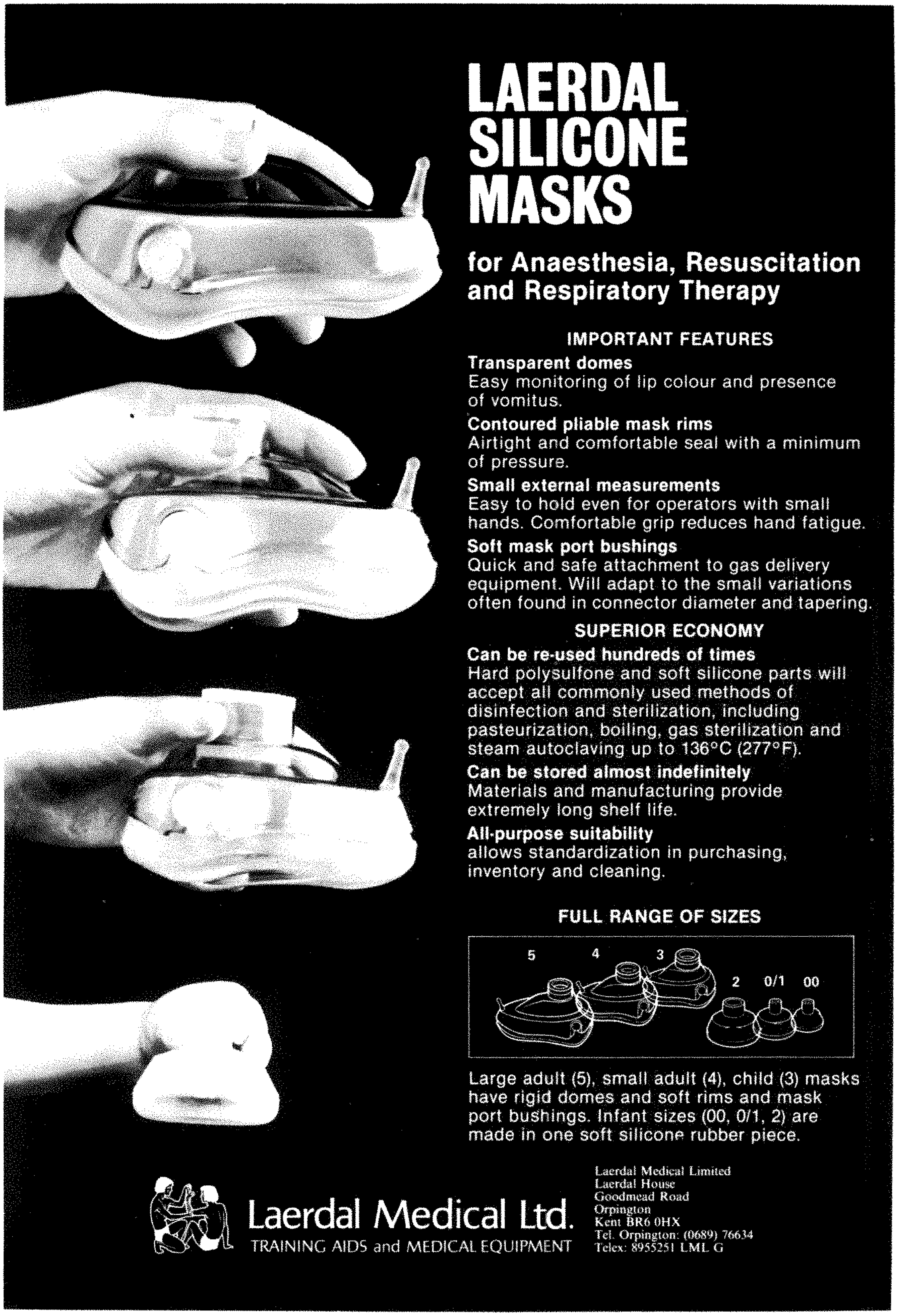

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Effect of varying F_IO_2 on pulmonary oxygenation indices: A computer simulation applied to well-known lung models *H. Toyooka, T. Sakamoto, M. Yamashita, M. Ogura, M. Sasaki, H. Tsutsumi, T. Aruga and K. Mii*
Hemodynamic and respiratory effects of epidural analgesia for gastrectomy in geriatric patients *Y. Kosaka, Y. Nishio, K. Matsui, K. Shiihara, M. Asano, H. Kawasaki, Y. Shimizu, M. Takasaki and A. Tanaka*
Pathological findings in a patient after long-term epidural administration of morphine *A. Fukuuchi and K. Yokoyama*

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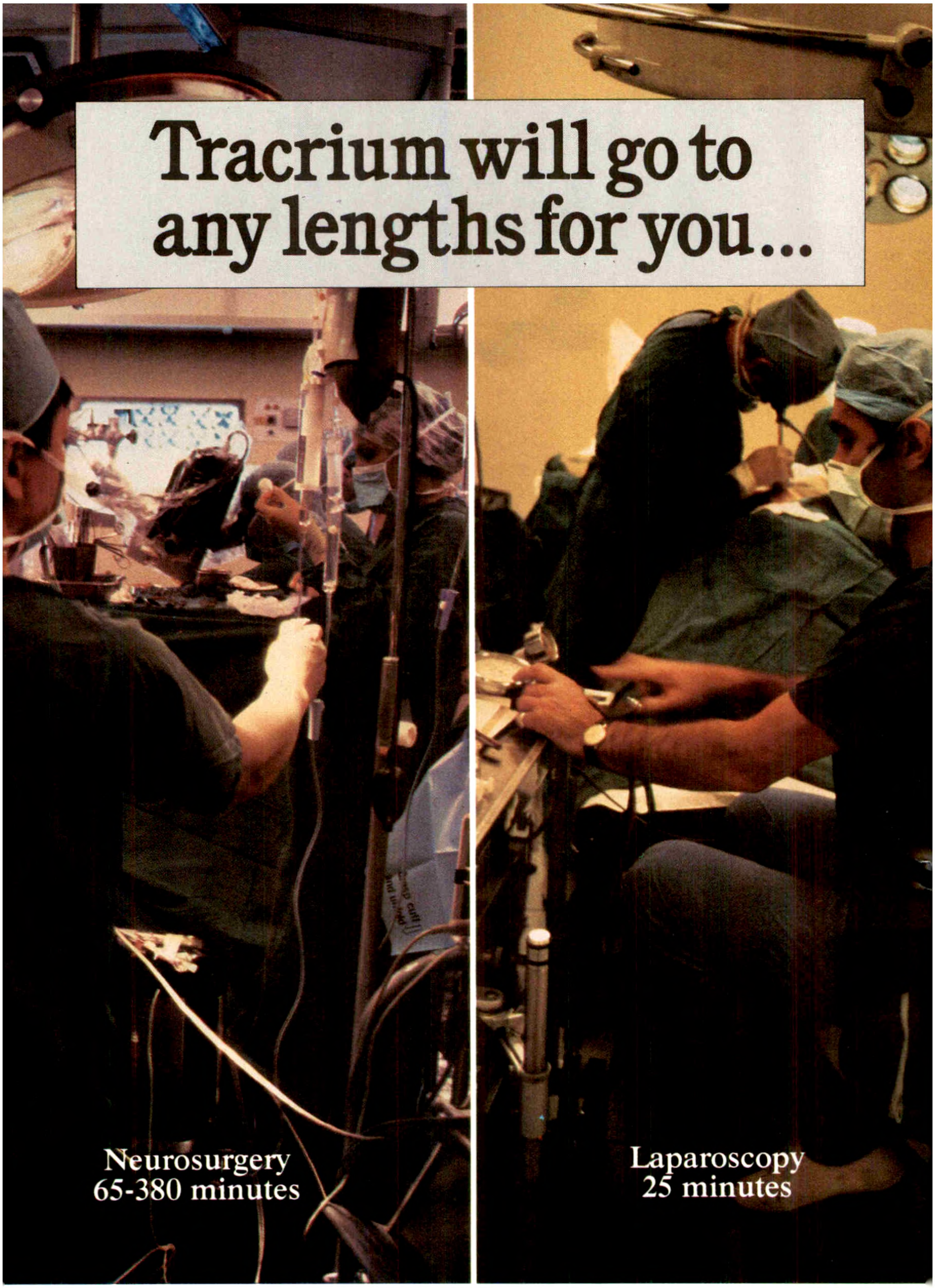

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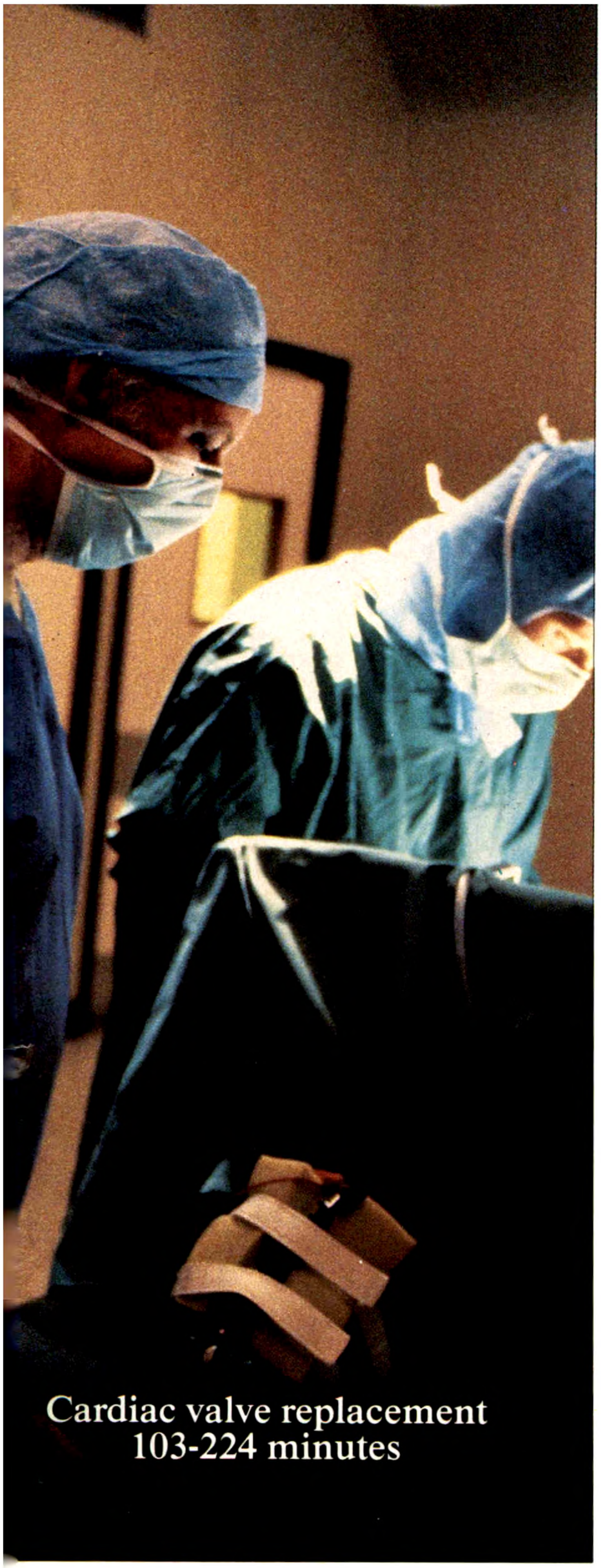

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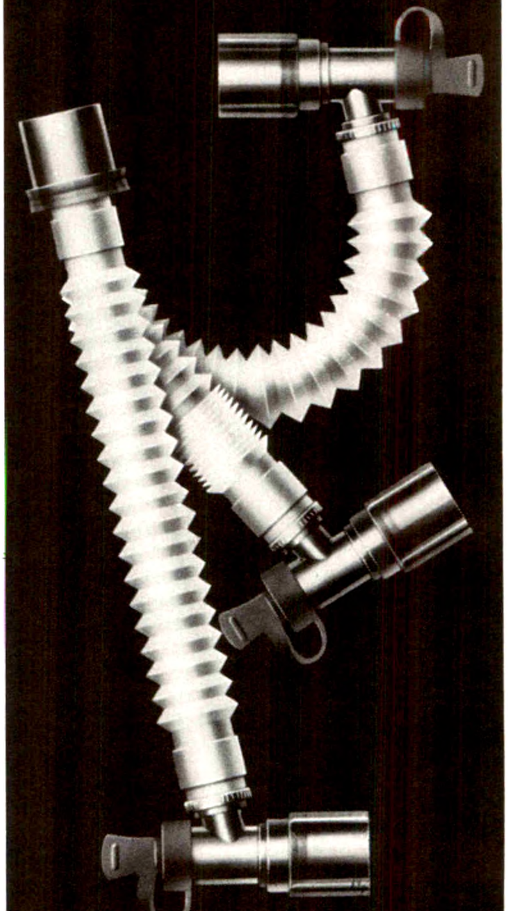

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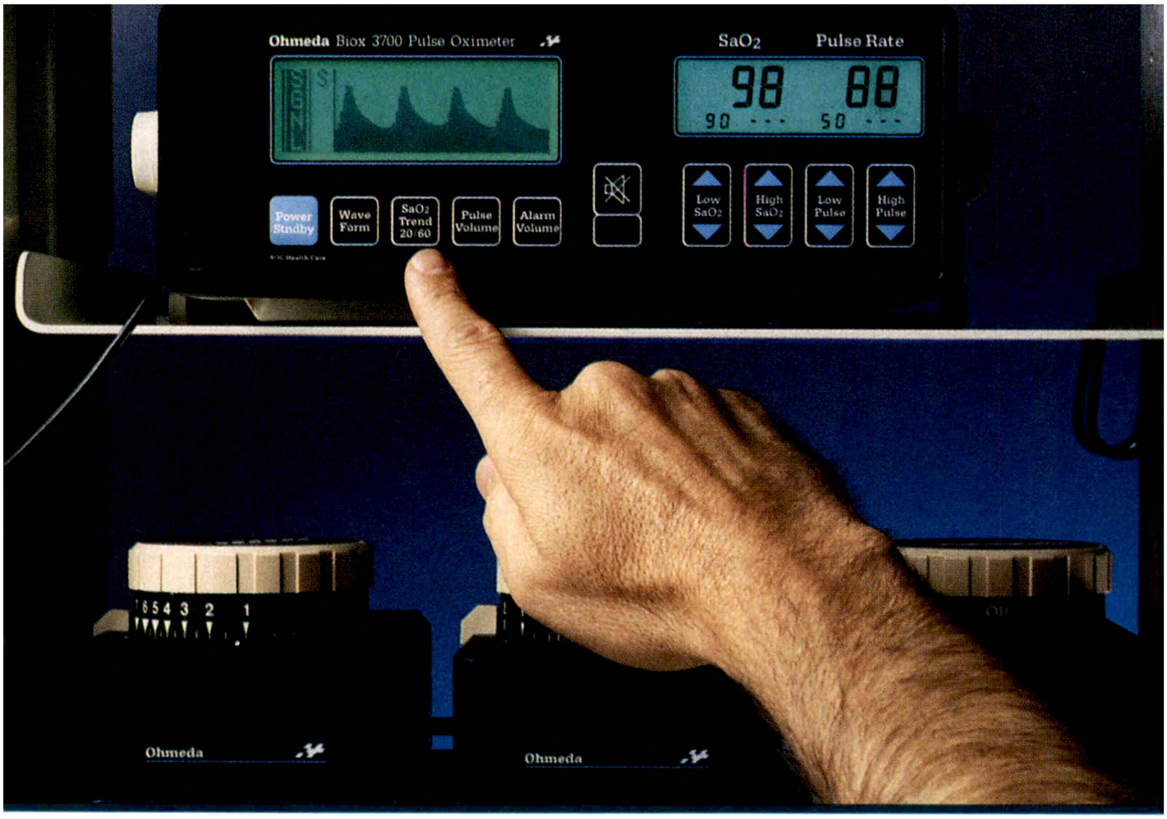

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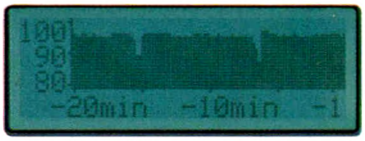

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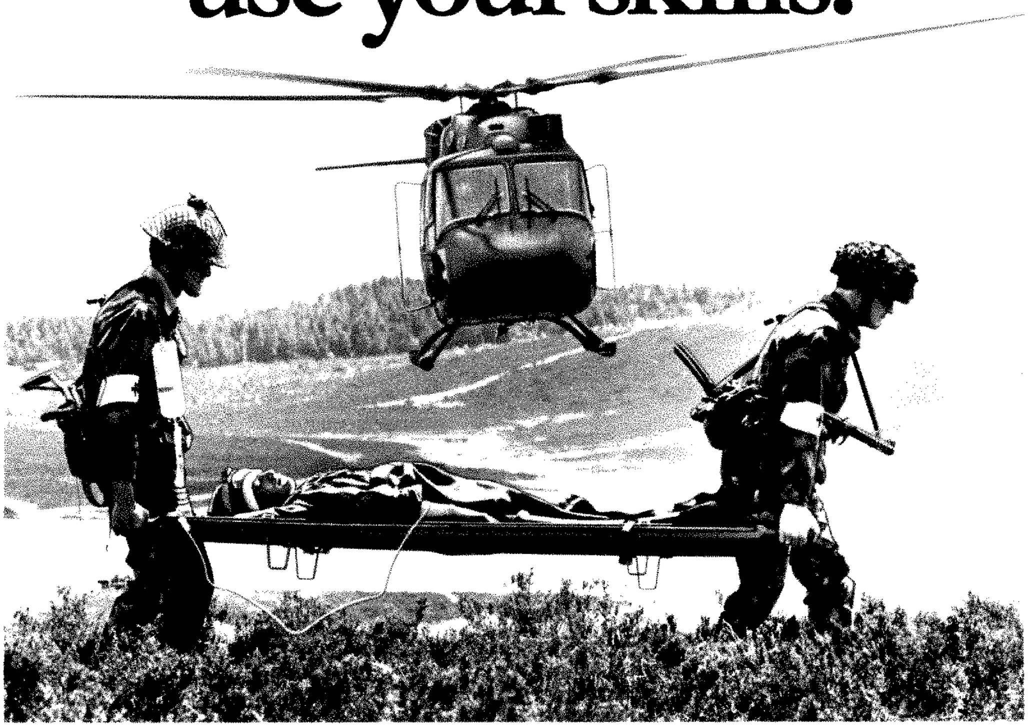

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Anaesthesia, 1986, Volume 41, pages 1085–1086

Editorial

The law and the practice of anaesthesia

Xenophobia, apart from its cultural undesirability, sometimes prevents understanding and appreciation of relevant events outside one's own country. Developments elsewhere in the world should not be ignored. If they are, it may on occasion be nothing more than short sighted, but on others it may be almost foolhardy. Some of the authors, for example, of letters in response to an earlier Editorial, which drew attention to the transatlantic problems of defensive medicine,[1] seemed to take a peculiarly insular view of events overseas which is not, in this writer's view, justified by recent history. Three general examples of recent developments overseas will suffice, but there are others.

The influence of financial profit, for hospitals and practitioners, on the ethical practice of hospital medicine in the United States of America is already causing great concern there; contracts which involve hours of work for hospital doctors at senior and junior levels in various European countries are now seen not necessarily to be to the benefit of patient or doctor; recent legislation of various overseas governments in relation to medical practice is far reaching in its potential effect. Each of these can be related to trends in this country and is therefore worthy of note because we do not have immunity from overseas influence.

Federal German law, enacted 1 January 1986 has now, with commendable thoroughness, laid down stringent criteria for the manufacturers of medical technical equipment, including the requirement for inbuilt systems of monitoring of the apparatus. Naturally, and perhaps rightly, this law is not confined to manufacturing detail but extends also to the users; thus, in that country, it is now against the law for a medical practitioner to use a device (Group 1 specifies inhalational anaesthesia apparatus and lung ventilators) unless he has been instructed in the proper use of the machine and has tested it before use. 'The person handling the equipment of Group 1 must satisfy himself/herself of the functional safety and perfect condition of the unit prior to handling it'. Now, that is the law in Germany. It is no longer a matter of professional practice, personal choice, or obsessionality. Quite how the law is to be enforced is not stated in the translation of the statutes which I have studied, but their implication is clear. There are, of course, similar criteria in British law, although here they are less formally, but nevertheless effectively, established by precedent and formal guidance.

Product liability is a matter which has hitherto not worried anaesthetists very much, but the Central Committee for Hospital Medical Services has prepared its response to new directives from the European Economic Community, which must be embodied in British legislation. This legislation appears to suggest that anaesthetists who make *ad hoc* mixtures of drugs in operating rooms or intensive care units may also come under the category of producer under the terms of these directives. It is also apparent that in the event of a user making a modification to apparatus, then the liability for safety and efficacy of the entire apparatus passes from the manufacturer to the inventor, who thus becomes a producer. The entire responsibility would thus devolve not on the actual manufacturer, but on the individual who made the modifications. One should remember that many near, and a few realised, disasters have happened because singular modifications have been made to equipment and a subsequent user has failed to understand what has been done. This law is designed to regularise the position and to define the extent to which manufacturers are involved, in order to limit their responsibility, but it may also create problems for innovators and initiators in medical developments. It would, additionally, give us some protection against the activities of maverick colleagues. The beneficiary is, however, the claimant who is provided with a clear route of action.

This gloomy catalogue must also include the fact that the Federal Drug Administration in the USA also has draft recommendations which require that anaesthetists should test their machines before use. The protocol lists no fewer than 23 tests, some of which have five parts. The contrasts between the attitudes

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(and presumably, the practice) of the doctors who have prepared the list and those of some, if not many, anaesthetists in this country, are indeed stark.

Do not think that even if you have followed the letter, and even the spirit of these edicts (which are surely meant to avert disasters), that you are free from threat from the law. The opinion has recently been expressed by a judge *in this country*[2] that, 'a heart does not stop under anaesthesia in the absence of negligence'. In the case in question, cardiac arrest occurred in a previously fit child and brain damage followed. The judgement was made on the basis of *res ipsa loquitur*, because the only other explanation presented was rejected by the judge as fanciful, while other more common causes would have been negligent acts on the part of the anaesthetist.

What is regarded as fanciful may, of course, change with the passage of time. The writer has been told stories about cases of malignant hyperpyrexia whose true diagnoses were unknown at the time of the legal action and, undoubtedly, what now seems to be a miscarriage of justice followed. It is possible that the same might have happened in cases of amniotic fluid embolism, retrolental fibroplasia, or anaphylaxis. We can now explain some, perhaps most, events and demonstrate causes even of historically fanciful events (status lymphaticus), thus, to state that, in the absence of any evidence of causation, and in the presence of a demonstrably high standard of care and attention (not shown to be present in the quoted case), that the anaesthetic is always responsible, and its administrator therefore negligent, seems peculiarly unhelpful.

Res ipsa loquitur thus has limitations which need to be clearly understood before the doctrine is assumed to apply widely to *any* cardiac arrest. If it were to be used indiscriminately, it would not only be anathema to the writer, but it would also be a threat to proper medical practice; sceptical agnosticism coupled with a healthy spirit of scientific enquiry seems a greatly preferable position for anaesthetists to adopt.

What is perceived to be negligent may also change with time. It is important in this respect, not only for anaesthetists individually to keep up to date, but also to be seen to do so. The relevance of peer review, or self assessment of performance against agreed criteria (our American friends call this Quality Assurance) should be viewed in this light. The Confidential Enquiry into Peri-operative Death is one such corporate and cooperative effort. Standards of contemporary practice are thus established and no-one need fear litigation so long as his standards match those of his peers.

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Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 12 December 1986 for April 1987, 13 March 1987 for July 1987 and 12 June 1987 for October 1987.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

Anaesthesia, 1986, Volume 41, pages 1087–1091

Topical nitroglycerin

A safeguard against pressor responses to tracheal intubation

S. KAMRA, J. WIG AND R. P. SAPRU

Summary

In order to attenuate the pressor response to intubation of the trachea we have studied the effects of 2% nitroglycerin ointment rubbed on the forehead approximately 12 minutes prior to intubation. A double blind, randomized design was used in 56 consecutive patients. Of these, 30 patients received the ointment while 26 patients formed the control group. The maximum rise in the systolic arterial pressure was significantly lower ($p < 0.001$) in the group (7.66 mmHg, 6.2%) as compared to the control group (25.7 mmHg, 20.2%). The rise in arterial pressure persisted for up to 4 minutes in the control group, but lasted for only one minute in the nitroglycerine group. The pulse rate, however, increased in both groups to an equal extent. We have found the application of 2% nitroglycerine ointment to be a safe, inexpensive, comfortable and effective means of attenuating the pressor response to intubation of the trachea.

Key words

Anaesthetic techniques; laryngoscopy, tracheal intubation.
Blood pressure; hypertension.

Significant haemodynamic changes, commonly observed following laryngoscopy and intubation, after induction of anaesthesia with a combination of barbiturate and suxamethonium, have been a cause of concern. These changes, which include a rise in systemic arterial blood pressure and pulse rate,[1] are at their peak approximately 30–45 seconds after laryngoscopy.[2] These changes have special significance in patients with cerebral and cardiovascular diseases since they may give rise to major complications such as left ventricular failure, acute myocardial infarction and cerebral haemorrhage.[3,4] Attempts to attenuate these responses by various drugs, or techniques, or their combinations have met with varied success.[5-12]

Nitroglycerin (NTG) a well known drug in the treatment of coronary artery disease, has also been used intravenously as an effective, short-acting hypotensive agent in cardiac and cerebral aneurysm surgery.[13,14] Nitroglycerin ointment has also been used to modify hypertension induced by electroconvulsive therapy.[15] Intranasal nitroglycerin, administered through a teflon cannula, has been shown to attenuate the pressor response following laryngoscopy and tracheal intubation.[10] However, as intranasal administration of the drug is somewhat cumbersome and may cause discomfort to the awake patient, we have evaluated the efficacy of topically applied NTG (2%) in attenuating the pressor response to laryngoscopy and tracheal intubation.

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Patients and method

Fifty-six healthy (ASA Class 1) patients of either sex, aged between 15 and 40 years, undergoing minor surgical procedures were included in this double blind randomised study. All patients were normotensive and had a normal ECG, haemoglobin and electrolytes pre-operatively. Informed consent was obtained from all the patients.

Patients were divided into two groups: C_1, the nitroglycerin-treated group (30 patients) and C_2, the control group (26 patients). The two creams used had similar consistency and colour. Premedication consisted of oral diazepam 0.15–0.2 mg/kg given the night before and again 2 hours before surgery. Morphine 0.1–0.15 mg/kg and promethazine 0.5–0.75 mg/kg were also given intramuscularly one hour prior to surgery. No anticholinergic drug was given either for premedication or at the time of induction of anaesthesia. On arrival in the operating theatre, the systolic arterial pressure (SAP) and pulse rate (PR) were recorded after a resting period of 2 minutes and designated B_1, pre-induction or basal value. Systolic arterial pressure was measured by means of a sphygmomanometer. A 5-cm length of ointment was applied by squeezing the contents of the pouch onto a specially designed dose measuring applicator supplied with the package; this was then spread and rubbed with the applicator, to cover an area of 10 × 5 cm over the forehead. The ointment was rubbed in to hasten its absorption and achieve adequate pharmacological effects. It was found after a few preliminary trials that the optimal pharmacological effects of the drug were seen 12–13 minutes after its application. To ensure a time gap of 12–13 minutes between application of the ointment and tracheal intubation, pre-oxygenation was commenced after the resting period of 5 minutes and was continued for a further 5 minutes.

Thiopentone 6 mg/kg was then administered and the SAP and PR at this time were designated B_2. Suxamethonium 2 mg/kg was given to facilitate tracheal intubation. The drug was removed with a gauze swab immediately following tracheal intubation. Any patient who strained or required a second attempt at intubation was excluded from the study. During laryngoscopy and intubation, SAP and PR were recorded. These recordings were continued every minute after tracheal intubation and designated I_1, I_2, I_3, I_4 and so on until spontaneous ventilation was established. Rate pressure product (RPP) was calculated from the corresponding observations of SAP and PR at the various intervals. The sequence of events is shown in Fig. 1.

During the period of apnoea, ventilation was carried out with 33% oxygen in nitrous oxide without the addition of any narcotic or inhalational agent. Since all patients were apnoeic for a minimum period of 4 minutes following suxamethonium injection (with the exception of a few who were apnoeic for 7–8 minutes), results were statistically analysed up to 4 minutes only. The Student's *t*-test was applied for analysis of the observations. Patients were observed for any skin rash and hypotension in the intra-operative period. Postoperatively, the patients were followed for 24 hours and the occurrence of nausea, vomiting, hypotension or palpitations recorded.

Results

Both groups were comparable with regard to their mean ages and weights (Table 1).

Systolic arterial pressure (SAP)

The maximum rise in SAP from the basal value in C_1 (NTG group) was 6.2% (7.66 mmHg) as compared to 20.2% (25.7 mmHg) in the control group (Table 2). This difference was highly significant ($p < 0.001$). In the NTG group (C_1) the

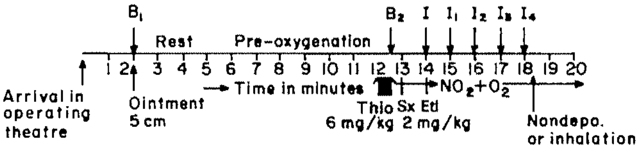

Fig. 1. Sequence of events of ointment application, induction of anaesthesia and timing of observations of systolic arterial pressure (SAP) and pulse rate (PR).

Table 1. Mean ages and weights in the two groups

Group	Age in years, mean (SD)	Weight in kg, mean (SD)
C_1 (30 patients)	26.16 (6.3)	50.8 (7.2)
C_2 (26 patients)	27.7 (6.1)	50.5 (8.1)
p	>0.05	>0.05

rise in SAP lasted for only 1 minute whereas in the control group (C_2) it lasted for more than 4 minutes (Table 3).

Patients in both groups were subdivided into four categories: a, b, c and d, depending upon the range of increase in SAP, i.e. $\leqslant 10$, 11–20, 21–30, and $\geqslant 30$ mmHg rise from the basal value. Fifty-seven percent of patients in the C_1 group had a rise of $\leqslant 10.0$ mmHg (category a) as compared to 11.5% of patients in the C_2 group (control). A rise of $\geqslant 30$ mmHg was observed in 61.5% of patients in the C_2 (control) group (category d), whereas none of the patients in the C_1 group showed a rise in this range (Table 4).

Pulse rate (PR)

A significant increase in pulse rate from the basal value was recorded in both groups; the maximum increase was 12.2% and 13.5% for C_1 and C_2 groups respectively. The increase in PR in the two groups was of a similar magnitude. The pulse rate had not returned to the basal value (B_1) even by the fourth minute in the post intubation phase in either of the two groups (Table 5).

Rate pressure product (RPP)

The maximum increase in RPP from the basal value (B_1) was found at one minute after intubation (I_1) in both groups. The RPP rise was more than double in the control group as compared to the NTG group (4397 and 2101 respectively).

Discussion

The action of topically applied 2% nitroglycerin ointment starts within 20 minutes and reaches a peak between 60–90 minutes.[16,17] A 2.5-cm length of 2% NTG ointment applied topically is equal to 15 mg of glyceryl trinitrate.[17] Each patient in our series received a 5-cm length of 2% ointment, thus corresponding to 30 mg of glyceryl trinitrate. The concentrations reached in the plasma after topical application are surprisingly high compared to those found after administration via the sublingual route.[18–20] However, skin absorption is affected by many factors, including area of application, cutaneous blood flow at the site of application, rate of evaporation and the dose.[16] We have

Table 2. Mean value (SD) of maximum increase in systolic arterial pressure (mmHg) with percentage increase, from basal (B_1) value, observed one minute after tracheal intubation (I_1) in the two groups

Group	B_1	I_1	Increase in mmHg from basal value	Percentage increase
C_1, mean (SD)	123.2 (11.77)	130.86 (13.62)*	7.66	6.2
C_2, mean (SD)	126.76 (11.79)	152.46 (22.13)*	25.7	20.2
p	<0.05‡	<0.001†		

*Statistically significant difference on analysis within the groups.
†Statistically significant difference on analysis between the groups.
‡No statistically significant difference on analysis between the groups.

Table 3. Systolic arterial pressure recordings, made at various intervals; pre-induction (B_1), after thiopentone (B_2), during intubation (I) and 1, 2, 3 and 4 minutes after intubation (I_1, I_2, I_3 and I_4 respectively) in the two groups

Group		B_1	B_2	I	I_1	I_2	I_3	I_4
C_1	Mean	123.2	115.2 *	130.13*	130.86*	124.67	122.2	122.13
	SD	11.77	15.34	11.66	13.62	12.91	13.94	14.28
C_2	Mean	126.76	114.15*	150.23*	152.46*	146.38*	140.85*	132.84
	SD	11.79	12.02	21.48	22.13	20.80	19.31	14.41
	p	>0.05‡	>0.05‡	<0.001†	<0.001†	<0.001†	<0.001†	0.001†

*Statistically significant difference on analysis within the groups.
†Statistically significant difference on analysis between the groups.
‡No statistically significant difference on analysis between the groups.

Table 4. Distribution of the magnitude of increase in SAP in the different groups

	a ≤10	b 11–20	c 21–30	d ≥30
	Number (%)	Number (%)	Number (%)	Number (%)
C_1 ($n=30$)	17 (56.66)	10 (33.33)	3 (10.0)	—
C_2 ($n=26$)	3 (11.5)	6 (23.1)	1 (3.8)	16 (61.5)

Table 5. Mean values (beats/minute) of pulse rate at various intervals; pre-induction (B_1), after thiopentone (B_2), during intubation (I) and 1, 2, 3 and 4 minutes after intubation (I_1, I_2, I_3 and I_4 respectively) in the two groups

Group		B_1	B_2	I	I_1	I_2	I_3	I_4
C_1	Mean	92.27	95.33*	101.46*	102.93*	103.13*	103.53*	103.13*
	SD	16.27	14.79	15.1	11.32	11.32	10.91	10.13
C_2	Mean	94.92	98.08*	107.46*	107.76*	105.76*	103.69*	102.53*
	SD	17.74	14.52	14.59	14.07	12.8	15.58	14.58
	p	>0.05†	>0.05†	>0.05†	>0.05†	>0.05†	>0.05†	>0.05†

*Statistically significant difference on analysis within the groups.

†No statistically significant difference on analysis between the groups.

applied a 5-cm length (equal to 30 mg of glyceryl trinitrite) over a very vascular area and rubbed it in to further hasten absorption. The basic idea of using any drug for attenuating the hypertensive response to tracheal intubation is that its peak effect should correspond to that of the stimulus. A 12–13 minute time gap was allowed between application of NTG and tracheal intubation in the study, as this time interval was found to be satisfactory after preliminary clinical trials. To the best of our knowledge, the time course of action of NTG ointment when applied and rubbed on the skin, has not been reported. However, NTG ointment has been used successfully for modification of ECT-induced hypertension,[15] although, in that study the drug was applied 45 minutes prior to ECT.

Intranasal NTG has been effectively used for suppressing the pressor response to tracheal intubation,[10] but the method adopted for administration of the drug appears cumbersome. We have also observed that the degree of tachycardia induced by NTG in the present study was less than that observed following intranasal NTG.

The rise in SAP following laryngoscopy and tracheal intubation was significantly less in NTG group as compared to the control group. However, pulse rate increased significantly and to a similar extent in both groups. The increase in RPP in the control group (C_2) was more than twice that observed in the NTG (C_1) group.

Apart from the suppression of the pressor response to tracheal intubation, NTG ointment may benefit the ischaemic myocardium by its known vasodilator properties, thus facilitating oxygen delivery to the myocardium.[21–25]

The previously reported side effects of NTG ointment,[16–17] such as headache, nausea, dizziness, nasal congestion, palpitations and hypotension were not observed in any of our patients during 12–24 hours postoperatively.

In conclusion, we suggest that the application of NTG ointment is a simple, cheap, effective and comfortable means of attenuating the pressor response to laryngoscopy and tracheal intubation.

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Oxygenation during electroconvulsive therapy

A comparison of two anaesthetic techniques

J. K. L. LEW, R. J. EASTLEY AND C. D. HANNING

Summary

Oxyhaemoglobin saturation was monitored continuously during electroconvulsive therapy in two groups of patients. All patients were anaesthetised using methohexitone (40–100 mg) and suxamethonium (25–50 mg). In group 1 (n = *48), the patients' lungs were ventilated manually with oxygen in air (40–50%) during the modified convulsion. In group 2 (n = 47), the convulsion was allowed to subside before recommencing manual ventilation with a similar gas mixture. Eight patients in group 1 and seven patients in group 2 received more than one shock and were excluded, leaving 40 patients in each group. In group 1, one patient had a minimum oxygen saturation of less than 90% after the electric shock as opposed to 11 in group 2 ($p < 0.01$). Five of the patients in group 2 had a saturation of less than 80%. It is concluded that patients undergoing electroconvulsive therapy should be ventilated with an oxygen-enriched gas mixture during the convulsion induced by the electric shock in order to avoid hypoxaemia.*

Key words

Anaesthesia; electroconvulsive therapy.
Complications; hypoxia.

Electroconvulsive therapy (ECT) is widely practised for the treatment of depression and schizophrenia. In the UK, approximately 200 000 treatments are administered annually.[1] The usual practice is for anaesthesia to be induced, followed by the administration of a short-acting muscle relaxant. Ventilation is controlled with oxygen-enriched air until the muscle relaxant is effective. The electric shock is then administered. No clear guidance is given in the literature concerning the subsequent management of the patient. Some anaesthetists commence manual ventilation immediately after the shock, whereas others allow the convulsion to cease before recommencing manual ventilation, which is then continued until the return of spontaneous respiration.

There are several factors that could lead to hypoxaemia. The patient is apnoeic and oxygen supply is discontinued momentarily during treatment, there may be some pre-existing lung disease and oxygen consumption will be increased by the muscular activity of the convulsion. ECT causes a brief but intense stimulation of the sympathetic nervous system, resulting in tachycardia and hypertension and thus increasing myocardial oxygen demand. Hypoxaemia may be detrimental in such a situation and should be avoided, particularly in the presence of ischaemic heart disease.

The aim of this study was to determine if hypoxaemia occurred during ECT and if it could be prevented or reduced by manual ventilation

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with oxygen-enriched air during the modified convulsion.

Method

The study was approved by the local ethical committee and verbal consent was obtained from all patients. Those who were too disturbed to give consent were excluded from the study. Ninety-five otherwise unselected patients were studied in two groups; group 1 consisted of 48 patients and group 2, 47. Each group was anaesthetised by one of two separate consultant anaesthetists, one of whom routinely performs artificial ventilation during the convulsion while the other does not.

The anaesthetic technique was standardised. On arrival at the ECT suite, patients were weighed and information was sought regarding their past medical history, smoking habits and medication. After a short explanation and with consent, an ear lobe was 'arterialised' by rubbing with an isopropyl alcohol swab and glyceryl trinitrate cream for about 30 seconds. The ear-piece from a pulse oximeter was attached to the ear lobe and a baseline oxyhaemoglobin saturation ($S\text{ao}_2$) recording obtained. Once a steady baseline was achieved after 30–90 seconds, anaesthesia was induced with methohexitone 40–100 mg and suxamethonium 25–50 mg injected into a vein in the antecubital fossa. The patient's lungs were ventilated manually using a self inflating (Ambu) bag with an inlet gas flow of 6 litres/minute oxygen, giving an inspired oxygen concentration of 40–50%. An oropharyngeal airway was used if required. When the fasciculations had subsided, manual ventilation was discontinued and a mouth gag inserted. The electric shock, either bilateral or unilateral, was then administered by the psychiatrist. Those patients to whom the electric shock was administered more than once to produce a convulsion were excluded from the study.

Manual ventilation with the same Ambu bag and oxygen flow was restarted immediately in the patients in group 1 and was continued throughout the modified convulsion until spontaneous ventilation returned in the patients in group 2. The convulsion was allowed to stop before restarting manual ventilation, which was continued until the return of spontaneous breathing.

Throughout the procedure, oxygen saturation was monitored continuously using a pulse oximeter (Ohmeda Biox III) and a continuous tracing was obtained on a chart recorder. Both instruments were calibrated according to the manufacturers' instructions. Accurate functioning of the oximeter was ensured by checking that the displayed pulse rate corresponded to that of the patient. The timing of each event was noted on the continuous chart.

The intensity of the convulsion was assessed according to the following classification modified from Ferguson.[2] Mild: movement of facial muscles; moderate: large joints, facial and minimal back movements; severe: above and marked back movements.

Statistical analysis was with the unpaired *t*-test, the Chi squared test (with Yates' correction) and Wilcoxon's rank sum test as appropriate.

Results

Anaesthesia and ECT were uneventful in all the patients studied. No difficulties were encountered with airway control or anaesthetic management. Eight patients in group 1 and seven in group 2 had the electric shock administered more than once to produce a convulsion and these were excluded from the analysis, leaving 40 patients in each group.

The two groups were comparable with respect to age, weight and sex (Table 1). There was no significant difference between the groups in smoking habits based on the case records and questioning. However, many of the patients were unwilling or unable to give much information and the data is necessarily incomplete. Four patients in group 1 and five in group 2 had a history of chronic obstructive airways disease.

The patients in group 1 received a larger mean dose of methohexitone than those in group 2 ($p < 0.01$). The dosage of suxamethonium was similar in both groups. Twenty-three patients in group 1 had bilateral ECT compared with 34 in group 2 ($p < 0.02$). However, there was no significant difference in the intensity or duration of the convulsion between the two groups. After induction, the patients in group 2 were pre-oxygenated earlier ($p < 0.01$) and for a longer period ($p < 0.05$). The time interval from discontinuing manual ventilation prior to the shock to restarting ventilation after the shock was markedly different, as would be expected ($p < 0.001$). The patients in group 1 were not

Table 1. Patient characteristics and anaesthetic data

	Group 1	Group 2	
No of patients (*n*)	40	40	
Age (years)			
Mean (SD)	52 (16)	58 (15)	NS
Range	20–77	21–78	
Weight (kg)			
Mean (SD)	59.1 (12.2)	61.8 (15.6)	NS
Range	38–84	43–113	
Sex			
Males	12	9	NS
Females	28	31	
Smoking			
No history available	15	14	
Smokers	16/25	9/26	NS
Dose of methohexitone (mg)			
Mean (SD)	63.2 (10.0)	54.4 (13.0)	$p<0.01$
Range	40–80	40–100	
Dose of suxamethonium (mg)			
Mean (SD)	32.9 (5.0)	31.1 (6.7)	NS
Range	25–50	25–50	

Table 2. Details of ECT

	Group 1	Group 2	
Type of ECT			
Bilateral	23 (57.5%)	34 (85.0%)	$p<0.02$
Unilateral	17 (42.5%)	6 (15.0%)	
Degree of convulsion			
Minimal	10	10	
Moderate	21	27	NS
Severe	8	3	
Duration of convulsion (seconds)			
Mean (SD)	36.0 (18.6)	38.1 (12.9)	NS
Time from methohexitone injection to start of manual ventilation (seconds)			
Mean (SD)	51.9 (7.9)	46.9 (8.7)	$p<0.01$
Duration of pre-shock oxygenation (seconds)			
Mean (SD)	15.9 (7.4)	19.0 (5.9)	$p<0.05$
Time from stopping ventilation before shock to restarting ventilation after shock (seconds)			
Mean (SD)	30.0 (5.9)	60.3 (12.0)	$p<0.001$

ventilated for a mean of 30 seconds as opposed to 60.3 seconds for those in group 2.

Both groups had a similar baseline $Sa\text{o}_2$ and had a small but statistically significant reduction after the administration of suxamethonium ($p < 0.005$) (Fig. 1, Table 3). The minimum $Sa\text{o}_2$ prior to the shock and the $Sa\text{o}_2$ immediately before the shock were similar in both groups. After the shock, $Sa\text{o}_2$ decreased in 24 patients (60%) in group 1 and in 33 patients (82.5%) in group 2. In all the other patients it was either unchanged or very slightly increased. Mean values are shown in Table 3 and Fig. 1. The distribution of minimum post shock $Sa\text{o}_2$ is shown on the histogram in Fig. 2. One patient in group 1 had a minimum $Sa\text{o}_2$ of less than 90%, whereas there were 11 in group 2 ($p<0.01$) of which five had an $Sa\text{o}_2$ of less than 80%.

Discussion

This study demonstrates that manual ventilation with oxygen-enriched air during the modified convulsion of ECT was effective in preventing hypoxaemia during that period. Over a quarter of the patients in group 2, where such ventilation

Table 3. Oxygen saturation (SaO_2) values

	Group 1	Group 2	
n	40	40	
Baseline SaO_2 (%)			
Mean	96.2	96.7	NS
Range	92–99	92–100	
Minimum pre-shock SaO_2 (%)			
Mean	94.1	93.8	NS
Range	82–98	76–98	
SaO_2 just before shock (%)			
Mean	97.1	97.0	NS
Range	93–99	86–100	
Minimum post shock SaO_2 (%)			
Mean	96.0	91.2	$p < 0.005$
Range	89–99	72–99	

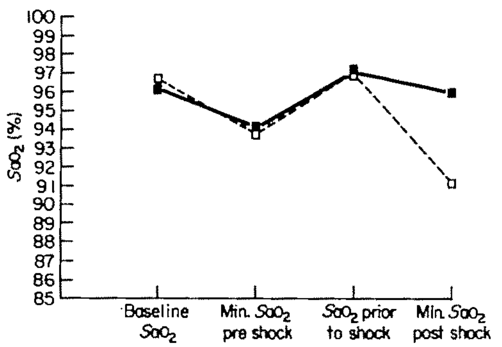

Fig. 1. SaO_2 changes during ECT. ■, group 1; □, group 2.

was omitted, had an SaO_2 of less than 90% (PaO_2 *c.* 8 kPa) during the convulsion. Five patients (12.5%) had an SaO_2 of less than 80%, corresponding to a PaO_2 of approximately 6 kPa. Most anaesthetists would regard a PaO_2 of 8 kPa as unacceptably low during routine anaesthesia.

The significance of transient hypoxaemia is open to question since the mortality during or immediately after ECT is low. Reviewing several papers, Marks[3] quotes an overall mortality of 0.16%. Morbidity after ECT, in contrast, is not so well documented. This is not surprising in view of the difficulty in quantifying morbidity. Any physical damage occurring during the treatment may not be apparent until much later, when it may be attributed to other causes.

The physiological changes which occur during ECT are well described.[3] There may be transient periods of bradycardia and hypotension, alternating with tachycardia and hypertension. This is attributed to the activation of the autonomic nervous system. It has been shown[4] that during ECT the rate pressure product can reach 35 000 with electrocardiographic changes of myocardial ischaemia. Many authors[5,6] believe that cardiovascular complications are the main cause of mortality during ECT modified with barbiturates and muscle relaxants as a result of the deleterious effect on the balance between myocardial oxygen supply and demand. Since myocardial oxygen demand is much increased during ECT, it is important not to compromise myocardial oxygen supply; adequate arterial oxygenation should therefore be maintained during the convulsion.

It has been postulated that asystole or bradycardia during ECT may result from inadequate ventilation.[7] This remains unproven, although our study suggests that this may be possible. Certainly, cardiac dysrhythmias during ECT occur most frequently after seizure activity[6] when, as we have shown, SaO_2 may be quite low.

Little guidance is given in the literature on ventilation during ECT. A recent survey carried out in Great Britain[1] has shown that a few clinics did not routinely administer oxygen. It has even been suggested that artificial insufflation can be entirely dispensed with during ECT.[8] Most authorities, however, including the Royal College of Psychiatrists,[9,10] recommend ventilation with oxygen-enriched air by facemask after induction, discontinuing ventilation during the shock and convulsion and then restarting manual ventilation until the return of spontaneous respiration.

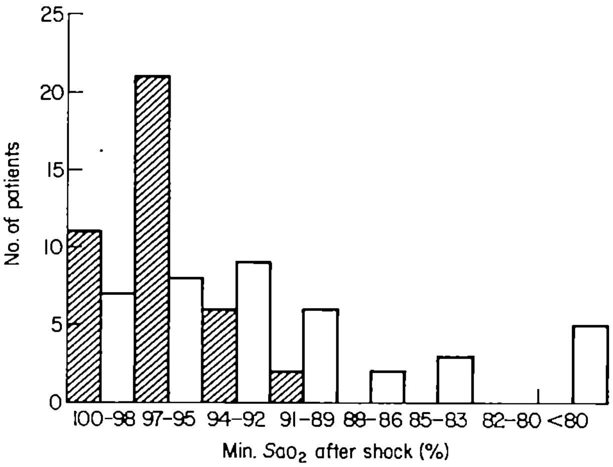

Fig. 2. Distribution of minimum Sao_2 following the electric shock. ■; Group 1; □, group 2.

None of the authors clearly recommend ventilation during the presence of convulsions. This attitude appears to stem from the work of Holmberg and others,[11] who found that continuous manual insufflation with oxygen during ECT prolonged the modified convulsion. However, their results are difficult to interpret in view of inconsistencies in methodology, such as the use of different anaesthetic agents and methods of measuring duration of convulsions. They concluded that prolonging the convulsion may improve the therapeutic outcome and is thus not necessarily disadvantageous. In our study, we could not find any difference in the duration of the convulsions between the two groups of patients.

In the present study, oxygen was added at a flow rate of 6 litres/minute to a self-inflating Ambu bag, delivering an inspired oxygen concentration of 40–50%. This system was selected because it was felt that it would be a better reflection of the practice in most units, where facilities for giving 100% oxygen may not be readily available.

Although the patients who required two or more shocks to produce a convulsion were excluded from the analysis, their recordings suggest that hypoxaemia in the group 2 patients was more marked when more than one shock was administered. This was not noticed in the group 1 patients. It is presumably a reflection of the longer period during which ventilation did not take place. However, the numbers were too small for any valid conclusions to be drawn.

All the patients in this study were anaesthetised by consultant anaesthetists and there were no airway problems. Under less ideal conditions, such as anaesthesia being administered by less experienced anaesthetists, airway obstruction and the administration of more than one electric shock, one might expect the hypoxaemia to be even more pronounced.

We conclude that unacceptable hypoxaemia may occur during anaesthesia for ECT. It can be prevented or decreased by ventilating the patients with oxygen during the modified convulsion.

Acknowledgments

We would like to thank Dr J. Wandless, Dr T. O'Carroll and the Psychiatric Staff for their help with the study. Our thanks also go to Ohmeda for the loan of the oximeter, Mr B. Ogden for his technical assistance, Professor G. Smith for his encouragement and constructive criticism and Miss J.M. Bowcutt for her patient secretarial assistance.

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Anaesthesia, 1986, Volume 41, pages 1098–1103

Ilioinguinal nerve block in children

A comparison with caudal block for intra and postoperative analgesia

S. J. MARKHAM, J. TOMLINSON AND W. R. HAIN

Summary

Fifty-two boys undergoing herniotomy, orchidopexy or ligation of patent processus vaginalis under general anaesthesia had supplementary analgesia; 26 had a caudal epidural block and 26 an ilioinguinal block. Analgesia was assessed both during and after surgery. Ilioinguinal block provides a useful alternative to caudal block.

Key words

Pain; postoperative.
Anaesthetic techniques; caudal, ilioinguinal.

There is a continuing search for satisfactory methods of pain relief after surgery. Techniques need to be safe, with a low incidence of side effects, reliably effective and to produce analgesia of adequate duration. It is also advantageous if the technique is simple and without later complications.

Caudal block using bupivacaine administered after induction of general anaesthesia but prior to surgery is widely used to provide analgesia during and after operation for lower limb surgery, circumcision and groin surgery in children. However, there is a risk of side effects with this technique,[1] such as motor block, bladder hesitancy and postural hypotension. Ilioinguinal block, for the relief of post herniotomy pain in children, has been advocated by both Shandling and Steward[2] and Smith and Jones.[3]

A blind, prospective study was undertaken to compare the quality of analgesia both during and after operation provided by these techniques. The incidence of side effects was also recorded.

Methods

Fifty-two fit boys (ASA 1) aged between 1 and 12 years due to undergo herniotomy, orchidopexy or ligation of patent processus vaginalis, were admitted to the study. The patients were age matched and randomly assigned to one of two groups, A or B. Group A patients were to have a caudal block and group B an ilioinguinal block. All patients were seen pre-operatively by the anaesthetist. Premedication consisted of oral diazepam 0.5 mg/kg to a maximum of 20 mg. The mood of each child was

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graded according to demeanour on a five-point scale at the pre-operative visit.[4]

Anaesthesia was induced with either intravenous thiopentone or by an inhalational technique using nitrous oxide, oxygen and halothane, as appropriate to the circumstances. Anaesthesia was maintained with nitrous oxide and halothane in oxygen, breathed spontaneously through a facemask; those patients who weighed less than 15 kg breathed through an Ayres' T-piece and the others through a Bain system.

Patients assigned to group A were turned to the left lateral position after induction of anaesthesia and a caudal block was performed using bupivacaine 0.5% plain. The volume used was one ml/year of age, plus 2 ml.[5] The patients in group B were left lying in the supine position; some had an ilioinguinal block performed by the anaesthetist, the others had the block performed by the surgeon after cleaning and draping. (This difference in technique was in response to the request of one of the two surgeons involved, who preferred that the local anaesthetic solution be injected near to the surgical field only after preparation for surgery.) The recommended dose of bupivacaine 0.5% for ilioinguinal block is 0.5 ml/year of age.[3]

The ilioinguinal block was carried out in all cases according to an accepted technique.[6] The pulse rate, arterial blood pressure, respiratory rate and halothane concentration were recorded on admission to the operating theatre, immediately after incision, at one-minute intervals for 5 minutes and at 5-minute intervals until the end of the operation. Postoperative observations were recorded by senior nursing staff completing questionnaires in the recovery room and on the ward. They were unaware of which block had been performed.

Questionnaires were completed on admission to the recovery room and 5, 10, 20 and 30 minutes later and also on admission to the ward and after 1, 2, 4 and 6 hours. The questionnaire included the observer's assessment of the child's pain using a 100-mm linear analogue scale with the extremes marked 'Obviously pain free' and 'Obviously in extreme pain'. Children of 4 years and over were asked 'Does it hurt?'. Whether the child was awake or asleep, the mood of the child and any relevant comments were also noted. A fresh questionnaire was filled in at each time interval and then placed in an envelope to lessen bias caused by knowledge of previous observations; the observers were different nurses who were unaware of the nature of the child's analgesia.

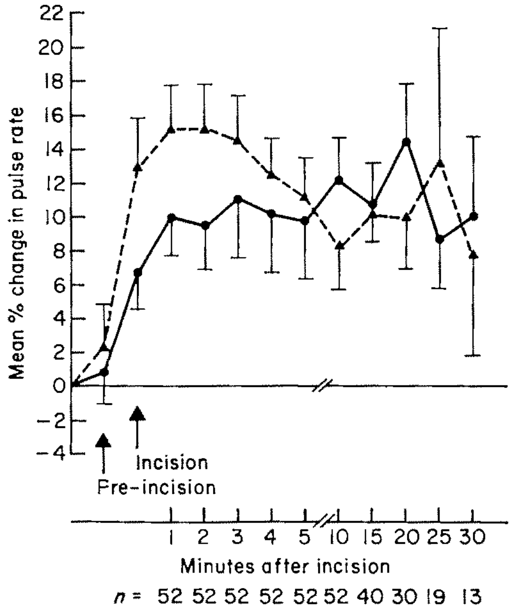

Fig. 1. Intra-operative changes in pulse rate, mean and standard deviation. ▲---▲, Caudal block; ●——●, ilioinguinal block. *n* = Number of children anaesthetised at that time; many operations had finished by 20 minutes.

The times at which postoperative analgesia (intramuscular diamorphine 0.1 mg/kg) was first used, when urine was first passed and when the child first walked unaided were recorded on the ward. Side effects such as vomiting, paraesthesia or haematoma formation were noted.

Results were analysed using Student's *t*-test, Chi squared and Wilcoxon's signed rank tests as appropriate.

Results

Figures 1 and 2 show the results of the intra-operative cardiovascular recordings. They show the mean changes in pulse rate and systolic blood pressure intra-operatively; these are recorded as the percentage change from that recorded on admission to the operating theatre. The mean pulse rate increased after the incision, more rapidly in group A, but by 5 minutes the increase was similar in the two groups, 10 to 15 beats/minute higher than the baseline. The increase in mean systolic blood pressure occurred more slowly than the rise in pulse rate and reached a maximum at 15–20 minutes after the incision.

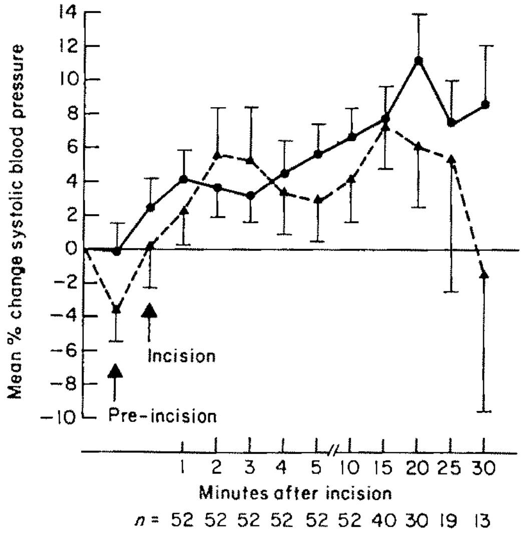

Fig. 2. Intra-operative changes in systolic blood pressure, mean and standard deviation. ▲---▲, Caudal block; ●——●, ilioinguinal block. *n* = Number of children anaesthetised.

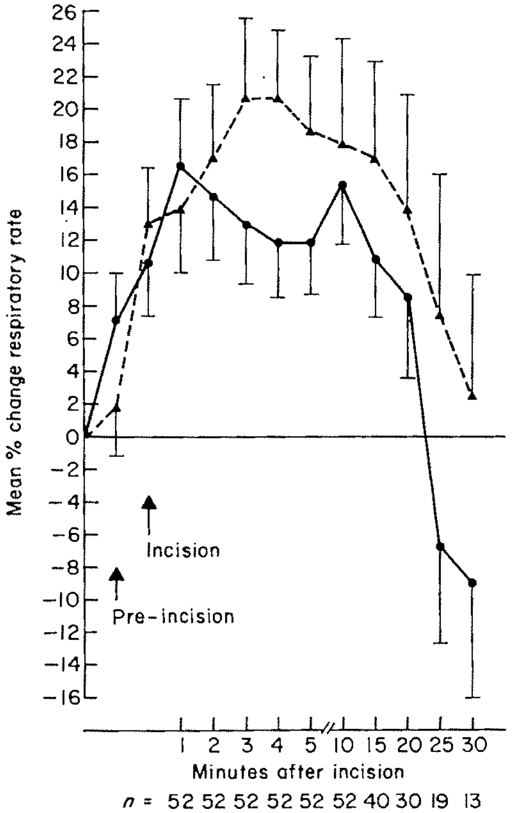

Fig. 3. Intra-operative changes in respiratory rate, mean and standard deviation. ▲---▲, Caudal block; ●——●, ilioinguinal block. *n* = Number of children anaesthetised.

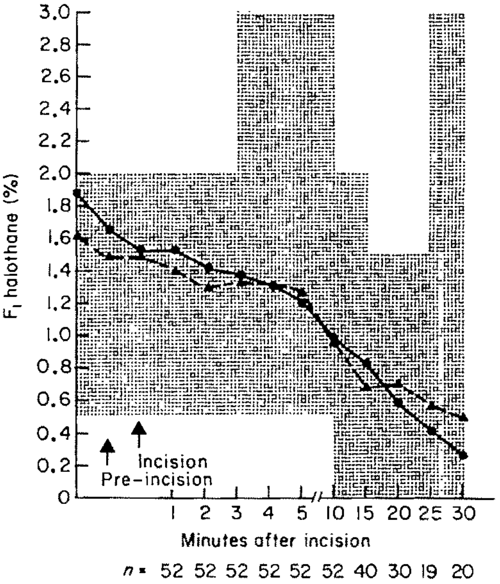

Fig. 4. Halothane concentration used throughout the operation, mean and range. ▲---▲, Caudal block; ●——●, ilioinguinal block. *n* = Number of children anaesthetised. The hatching indicates vaporizer concentration from uncalibrated Fluotec III vaporizers.

Figures 3 and 4 show the changes in respiratory rate and halothane concentration. The mean respiratory rate increased in both groups in response to the incision, remained elevated for about 10 minutes and then decreased towards the end of the procedure. The halothane concentration was altered by the anaesthetist in response to the clinical response and was similar in the two groups.

Statistical analysis of these results shows no significant difference in any of the values between the two groups. Figures 5, 6 and 7 show the results of the postoperative assessment.

The mean length of the linear analogue recorded in the recovery room and on the ward are shown in Fig. 5. Analysis, using Wilcoxon's signed rank test, reveals a statistically significant difference in the mean length between the two groups on admission to the recovery room only (time 0). The linear analogue lengths were otherwise similar throughout at about 20 mm.

Figure 6 shows the results of direct questioning. There was never a statistically significant difference in the numbers who complained of pain between the two groups. The mood of each patient was assessed in an attempt to correlate any consistently high linear analogue pain score

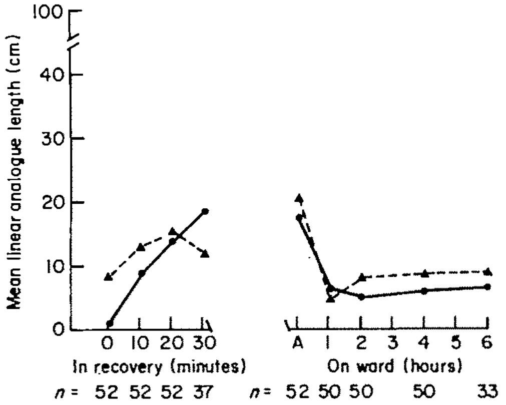

Fig. 5. Mean linear analogue lengths postoperatively. ▲---▲, Caudal block; ●——●, ilioinguinal block. n = Number of children on the ward at that time; some had left by 4 and 6 hours after surgery.

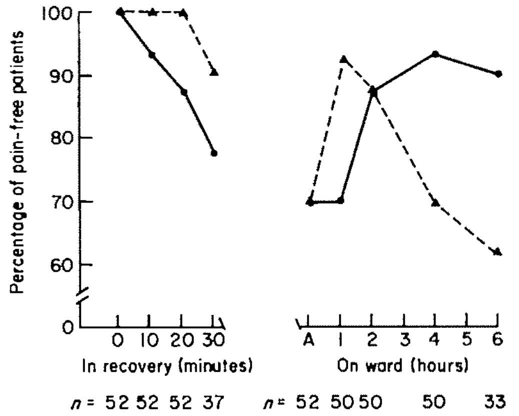

Fig. 6. Analgesia provided by the blocks shown as the percentage of pain free patients. ▲---▲, Caudal block; ●——●, ilioinguinal block. n = Number of children on the ward.

with a poor pre-operative demeanour. Figure 7 shows the mean linear analogue lengths of the patients with different mood scores (A, B) or (C, D or E). The difference exhibited was not statistically significant.

The incidence of complications is shown in Table 1. Three patients who had had a caudal block were given additional postoperative analgesia. One of these patients was given additional analgesia despite being accorded a linear analogue of less than 15 mm. Having been given additional analgesia these patients were excluded from further statistical analysis. No patient in group B (ilioinguinal block) was given

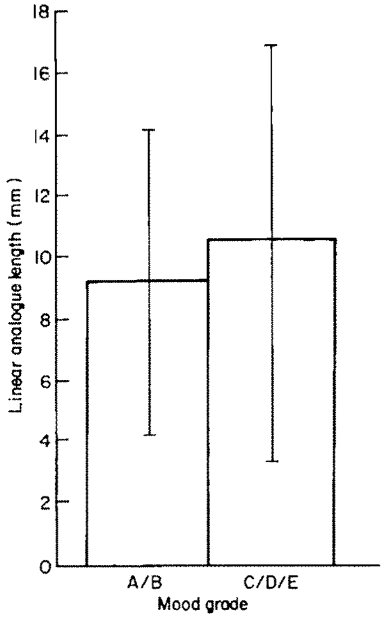

Fig. 7. Comparison of the linear analogue lengths (mean and standard deviation) between those with a good (A/B) and those with a poor (C/D/E) pre-operative demeanour.

additional analgesia. This difference between the groups did not reach statistical significance. Three patients in group A and 5 in group B vomited and one patient in each group was pyrexial postoperatively. Fifty-four percent in group A and 28% in group B had not walked by 6 hours. Nine patients were kept in bed for medical reasons and were therefore excluded from analysis. The only complication in which the difference between the groups was statistically significant concerns passage of urine postoperatively. Twelve of the caudal and 5 of the ilioinguinal group had not passed urine 6 hours after the operation ($p = 0.05$).

Discussion

The abolition of the cardiovascular response to pain, in particular the change in heart rate, by an anaesthetic agent, has been used as a measure of the adequacy of that dose of anaesthetic agent in the prevention of the perception of pain.[7] We assumed that all the children were similarly anaesthetised since the durations of anaesthesia were similar, the pulse rates, blood pressures and ventilation were stable and the pupils were central and small at the time of the incision. We used this

Table 1. Incidence of postoperative complications

	Group A (caudal) $n=26$ (%)	Group B (ilioinguinal) $n=26$ (%)	
Required postoperative analgesia by 4 hours	3 (11)	0 (0)	
Vomited	3 (11)	5 (19)	
Pyrexia	1 (4)	1 (4)	
Not walking at 6 hours*	12 (54)	6 (28)	
Not passed urine by 6 hours	12 (46)	5 (19)	($p<0.05$)

*Four patients in group A and five in group B were instructed to stay in bed.

same response as a measure of the analgesia provided by the local blocks. Pain assessment using linear analogues completed by nurse observers may not be ideal, since analgesic premedication, the presence or absence of parents and other factors may affect the child. Nevertheless, they have been used in this way before, by ourselves[4] and by other workers.[8-10] One patient in this study received additional analgesia despite the fact that the linear analogue at the time indicated otherwise.

Both techniques in this study seem to give similar freedom from pain. There is a suggestion in the results, not confirmed by statistical analysis, that ilioinguinal block has an earlier onset of action. Postoperative analgesia as assessed by observers using the linear analogue scale appeared satisfactory in both groups, with mean linear analogue lengths near or below the suggested threshold of 20 mm.[8] Most of the complications were seen more frequently in the caudal group, but only in the delay in the time to micturition was there statistical support for the supposition that ilioinguinal may be preferable to caudal block. The patients were neither actively encouraged to pass urine, nor was there any complaint of difficulty so the clinical significance of this difference is doubtful. The total dose of bupivacaine during an ilioinguinal block is less than that used for a caudal block. Studies are in progress to compare the incidence of complications following caudal blocks performed alternatively with similar volumes of 0.5 and 0.25% bupivacaine.

This study does not show whether a caudal or ilioinguinal block has significant advantages over using no local block. Postoperative pain after herniotomy often appears to be slight, particularly when a narcotic drug has been given before or during surgery. Other studies of pain after circumcision[4,8-10] have been challenged by Martin,[11] who belives that caudal blocks are not worth the time, risk or expense involved. Nevertheless, children are often more frightened of an intramuscular injection than of continuing pain and nurses are often reluctant to give narcotics postoperatively.[12] Such considerations, together with the enthusiasm of the recovery room staff and the receipt of letters of thanks from parents, encourages us to believe that these blocks are of value.

Acknowledgments

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Anaesthesia, 1986, Volume 41, pages 1104–1111

Buccal morphine premedication

A double-blind comparison with intramuscular morphine

A. P. FISHER, P. VINE, J. WHITLOCK AND M. HANNA

Summary

Fifty patients were admitted to a double-blind, double-dummy study comparing buccal morphine 10 mg tablets and intramuscular morphine sulphate 13.5 mg as premedication. This investigation was performed on the basis of favourable results obtained in an earlier 25 patient pilot study designed to examine the efficacy, safety and patient acceptability of buccal morphine 10 mg tablets as pre-anaesthetic medication. Both studies and sets of results are presented and show that, whilst buccal morphine is a safe alternative means of delivering opioid premedication, which is acceptable to the majority of patients, an equivalent intramuscular morphine dose is nevertheless a more effective premedicant in terms of anxiolysis and wakefulness, as assessed by linear analogue scores. Pharmacokinetic considerations are advanced both to explain the differing clinical efficacies of the two means of morphine administration and to indicate that improved per- and immediate postoperative analgesia might be obtainable in patients premedicated with buccal morphine.

Key words

Premedication.
Analgesics, narcotic; morphine.

Opioid premedication is generally administered intramuscularly, although there are practical and potential alternatives, for example oral sustained release morphine tablets,[1-3] morphine suppositories[4] and sublingual buprenorphine.[5,6]

De Boer *et al.*[7] have recently reviewed the subject of drug absorption by sublingual, buccal and rectal routes. Avoidance of first pass metabolism is an advantage enjoyed by all three routes, as is the ability to terminate drug absorption if necessary. Rectal absorption can be compromised by faecal content or evacuation and patient acceptability may be a problem. Sublingual and buccal routes would appear to have an advantage in terms of convenience and aesthetics of administration, and avoidance of injection, but maintenance of drug in these areas may be a variable problem depending on the formulation and saliva flow. With either route, tablet disintegration and residence time in the mouth are likely to be affected by eating and drinking. The buccal route involves the tablet being located on the mucosa of the gum above the gingival margin in the upper buccal sulcus and hence is less likely to be affected by talking or the accumulation of saliva on the floor of the mouth than is the sublingual route.

Buccal morphine is a recently developed formulation with a pharmacokinetic profile similar to that of intramuscular morphine; the

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buccal formulation is somewhat more bioavailable.[8,9] A pilot study was undertaken as an initial assessment of the potential of buccal morphine as premedication. As an examination of a new formulation, this was conducted as an open study, but favourable results indicated that a double-blind comparison with an established route of administration should be made. Both studies were conducted with the approval of the hospital ethical committee.

Methods

Fifty patients, ASA grade 1 or 2 who were not being treated with narcotic analgesics or other sedative or anxiolytic drugs and scheduled for elective surgery, were admitted to the study. On admission, each patient was assigned a trial number in a random fashion ensuring the receipt, at premedication, of the contents of an identically numbered packet. Each packet held a buccal tablet and an ampoule, the contents of which were for intramuscular injection. Within a packet, either the buccal tablet contained 10 mg morphine base, in which case the injection was placebo, or the buccal tablet was placebo, in which case the injection consisted of 13.5 mg morphine sulphate. In the pilot study, 25 patients fulfilling the above admission criteria were premedicated with buccal morphine 10 mg.

On the day prior to surgery each patient's informed, written consent was obtained, the use of linear analogue scales explained and a record made of patient height, weight, baseline blood pressure and heart rate. On the day of surgery, 90 minutes before the estimated time of induction of anaesthesia, measurements and assessments were made as follows: blood pressure, heart rate and respiratory rate (pilot study only); the patient also indicated levels of anxiety and wakefulness on two independently presented linear analogue scales, each consisting of a 10-cm horizontal straight line, marked at each end 'no anxiety', 'extremely anxious' and 'extremely drowsy', 'wide awake', respectively.

Premedication was administered after completion of these observations, which were subsequently repeated by the same observer at 15, 30, 60 minutes and in the anaesthetic room at 90 minutes. Sleeping patients were not disturbed. Patient acceptability was assessed preoperatively by recording any spontaneous observations made by the patient concerning the tablet or injection and, unless the patient was asleep, by asking, 'Does the treatment suit you? Has it upset you in any way?'. Any unwanted effects were noted. Patients were questioned directly about nausea or vomiting.

At induction of anaesthesia, patients were examined to confirm the continued presence of the tablet. Details of the anaesthetic and patient vital signs peroperatively were recorded, including the respiratory rate of spontaneously breathing patients, further opioid administration and time to awakening following discontinuation of the anaesthetic. Anaesthetists were asked to record any complications encountered or observations they wished to make concerning the anaesthetic course.

Postoperatively, recordings were made of patient vital signs in recovery and on the ward, the incidence of nausea and vomiting and the time to first administration of postoperative analgesia. On the first postoperative day, a visit was made to re-assess the acceptability to the patient of the two routes of drug administration, to elicit any preference for one or other route alone, to record any unwanted effects and to examine the buccal mucosa.

A paired t-test was used in both studies to detect any statistically significant intragroup changes from baseline values of vital signs, anxiety and wakefulness scores during the premedication period. In the double-blind study an unpaired t-test was used to detect any statistically significant intergroup differences in anxiety and wakefulness scores at each assessment.

Results

Demographic data

From the initial group of 25 patients in the pilot study, one female was withdrawn at 60 minutes due to displacement of the tablet. Data on three patients in the double-blind study were lost. The demographic data relating to the two studies are shown in Tables 1 and 2 respectively.

Table 1. Pilot study demographic data (mean, range)

Age (years)	43 (18–76)
Weight (kg)	68 (49–104)
Height (cm)	170 (150–188)

Table 2. Double-blind study demographic data

	Active tablet ($n = 22$)	Active injection ($n = 25$)
Patient details		
Age (years, mean SEM)	40.04 (2.34)	45.17 (2.85)
Weight (kg, mean SEM)	66.02 (1.67)	65.98 (2.41)
Height (m, mean SEM)	1.67 (0.02)	1.67 (0.02)
Male: Female	5:17	7:18
Operation details		
Hysterectomy	5	5
Tubal surgery	2	3
Colposuspension	2	3
Laparoscopy	1	2
Cholecystectomy	3	1
Varicose veins	4	3
Haemorrhoidectomy	1	1
Herniorrhaphy	1	2
Other	3	5

Vital signs

There were no statistically significant changes detected in blood pressure, heart rate or respiratory rate over the premedication period. In addition to the stability of vital signs shown statistically for the group, it was also noted that there were no clinically significant changes in individual patients. In particular, there was no respiratory depression as assessed by respiratory rate.

Anxiety

For each assessment, group mean linear analogue anxiety scores were plotted against time (pilot study, Fig. 1; double-blind study, Fig. 2). In the pilot study, statistically significant reductions in linear analogue anxiety scores were detected at 15, 30 and 60 minutes, but not in the anaesthetic room, by comparison with baseline level. In the double-blind study, statistically significant reductions in anxiety were detected at 30 minutes in the active tablet group and at 15, 30 and 60 minutes in the active injection group. There was a significantly greater anxiolytic effect in the active injection group at 15 minutes and in the anaesthetic room, although in neither group was there a significant difference between baseline and anaesthetic room anxiety levels.

Wakefulness

Data were processed in the same way as for anxiety data (pilot study, Fig. 3; double-blind study, Fig. 4). In both studies, and in all groups, statistically significant decreases in linear analogue wakefulness scores, by comparison with baseline, were detected at all assessment times. In the double-blind study, the reduction in wakefulness was significantly more marked at all assessments in the active injection group.

Peroperative course

There were no untoward complications peroperatively. The buccal tablet was found to pose no aspiration risk. There was no undue respiratory depression in spontaneously breathing patients. Two anaesthetists commented upon excessive salivation at reversal. Suction at this stage occasionally removed buccal tablet residue. Time to awakening was not clinically prolonged.

Patient acceptability

Data relating to the incidence and nature of unwanted effects peri-operatively are shown in Tables 3 and 4 for the pilot and double-blind studies respectively. Table 5 (double-blind study) shows the acceptability to patients of the two routes of administration and their preferences for one or other route.

Discussion

The advent of a buccal formulation of morphine requires that its potential usefulness in anaesthetic practice be assessed. An initial comparison of buccal with intramuscular morphine in post-

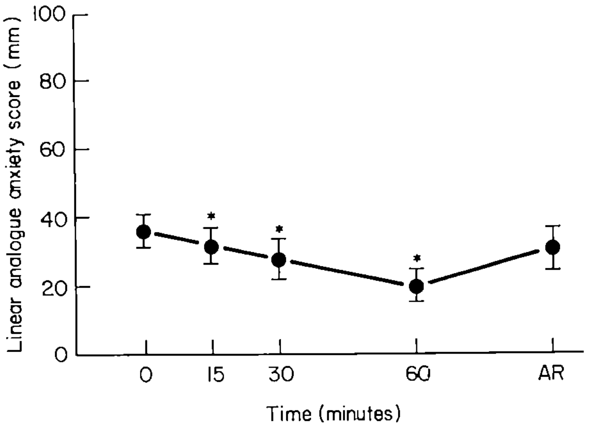

Fig. 1. Pilot study. Changes in anxiety as shown by linear analogue scores (mean, SEM). AR, Anaesthetic room (*c.* 90 minutes); *, $p < 0.05$ (paired *t*-test, $n = 24$).

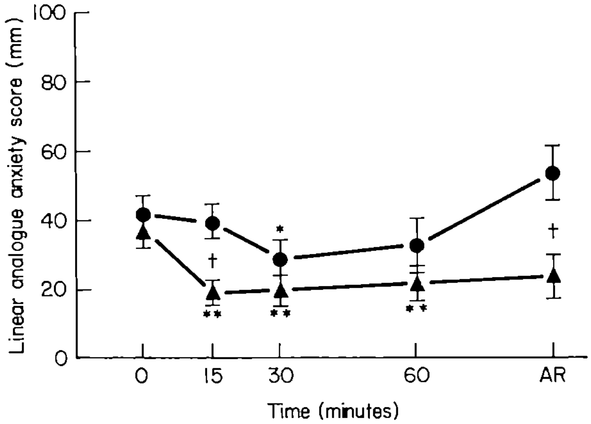

Fig. 2. Double-blind study. Changes in anxiety as shown by linear analogue scores (mean, SEM). AR, Anaesthetic room (*c.* 90 minute); ●, active tablet group ($n = 22$); ▲, active injection group ($n = 25$); *, $p < 0.05$; **$p < 0.01$, (paired *t*-test intragroup); †$p < 0.05$ (unpaired *t*-test intergroup).

Table 3. Pilot study. Unwanted effects and acceptability ($n = 24$)

Pre-operative	
Unwanted effects	7 (29.2%)
Nausea	0 (0.0)
Vomiting	0 (0.0)
Taste	5 (20.8%)
Headache	2 (8.3%)
Postoperative	
Nausea, vomiting	9 (37.5%)
Taste	12 (50.0%)
Mucosal abnormalities	0 (0.0)
Tablet acceptable	20 (83.3%)

operative pain control has been made by Bell *et al.*[9] Whilst more specifically anxiolytic drugs than morphine are available and potent, rapidly acting analgesics may be administered intravenously at induction of anaesthesia, it is still common practice to premedicate patients with opioids.

The difficulties inherent in the quantification of the subjective experience of anxiety have long been appreciated and the problem has been reviewed by Norris.[10] Wassenaar *et al.*[11] reported the use of the Multiple Affect Adjective Check

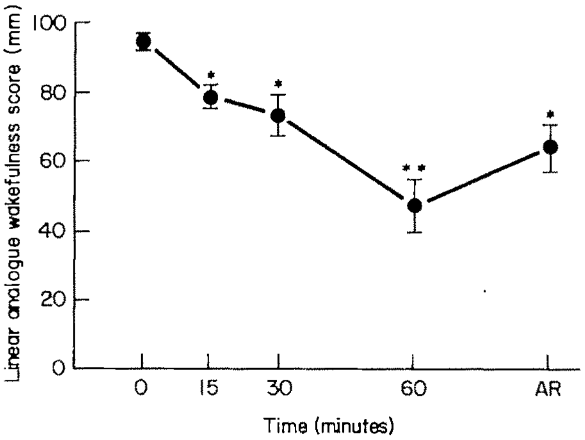

Fig. 3. Pilot study. Changes in wakefulness as shown by linear analogue score (mean, SEM). AR, Anaesthetic room (*c.* 90 minutes); *p < 0.05; **, p < 0.001 (paired *t*-test, *n* = 24).

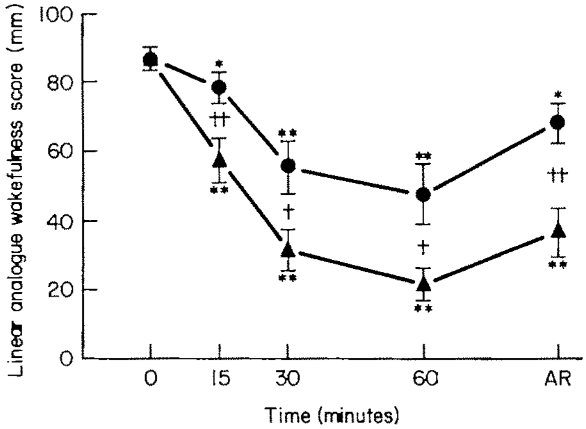

Fig. 4. Double-blind study. Changes in wakefulness as shown by linear analgoue score (mean, SEM). AR, Anaesthetic room (*c.* 90 minutes; ●, active tablet group (*n* = 22); ▲, active injection group (*n* = 25); *, p < 0.05; **p < 0.001 (paired *t*-test intragroup); †, p < 0.05; ††p < 0.001 (unpaired *t*-test intergroup).

List (MAACL) as devised by Zuckerman[12] in the assessment of pre-operative anxiety, and recently Elliott *et al.*[13] found a strong correlation between anxiety scores as measured by MAACL and linear analogue scores. Fell *et al.*,[14] in assessing the value of plasma catecholamine concentration measurement as an objective index of anxiety, have produced data which support the use of the linear analogue score as a measure of anxiety in the pre-operative patient.

The linear analogue score method was used in these studies because of the simplicity of the technique, coupled with the minimum of disturbance to the patient. In both studies, the linear analogue scores showed progressive reduction in anxiety and wakefulness following administration of buccal morphine. Statistical analysis of the scores showed these reductions to be significant. However, the double-blind study showed that intramuscular morphine appeared to have a more profound effect of quicker onset by comparison with buccal morphine and the increase in anxiety

Table 4. Double-blind study. Unwanted effects

	Number of patients		
	Active tablet		Active injection
	$n = 22$		$n = 25$
Pre-operative			
Unwanted effects	10 (45.4%)		7 (28.0%)
Nausea	1 (4.5%)		4 (16.0%)
Vomiting	0 (0.0%)		1 (4.0%)
Taste	4 (18.2%)		0 (0.0%)
Headache	4 (18.2%)		2 (8.0%)
Painful injection site	4 (18.2%)		1 (4.0%)
Postoperative	$n = 22$		$n = 24$*
Nausea	16 (72.7%)		13 (54.2%)
Vomiting	6 (27.3%)		11 (45.8%)
Taste	18 (81.8%)	$p < 0.001$	2 (8.3%)
Mucosal abnormality	0 (0.0%)		0 (0.0)

*One patient discharged home prior to postoperative assessment.

and wakefulness observed in the anaesthetic room was less marked in the active injection group.

The variability of response to the active tablet between patients was marked; some patients were apparently minimally affected whilst others were asleep at 60 minutes. Some of this variability may be ascribed to differing sensitivity of individuals to opioids, but it is likely that there was also variable rate of absorption of the drug.

Greatest depression of anxiety and wakefulness was found to occur at 60 minutes, which parallels the time to peak plasma morphine levels as measured in a kinetic study,[8] but our result must contain a methodological component in that the assessment subsequent to that at 60 minutes took place in the anaesthetic room after a disturbing journey through the hospital corridors, which, one assumes, can only increase anxiety and wakefulness.

Although any relationship between plasma levels of morphine and central nervous system effects may not be simple in view of the poor lipid solubility of the drug, the difference between the performances of the buccal and intramuscular preparations may find some explanation on the basis of the pharmacokinetic data available from the work of Bell *et al.*[9] They found that the plasma morphine level rose more quickly and to a higher peak value at about one hour after intramuscular administration, whereas after buccal administration a lower peak was achieved at between 1 and 2 hours. Such kinetic differences occurring over the 90 minute premedication period of our study could well be expected to produce disparate degrees of clinical effect.

In addition, there are three factors to consider which may have impaired the performance of the tablet in our investigation. Firstly, any tendency to dryness of the mouth due to pre-operative anxiety may decrease the early bioavailability of buccal morphine because of retarded adherence and solubilisation at the mucosa. Secondly, Bell *et al.*[9] report that 'the tablets were usually moistened (to facilitate their adherence to the mucosa)'. This manoeuvre was not employed in our studies. Thirdly, they used placebo buccal tablets to familiarise their patients with the route of administration prior to the study, which we omitted on the basis that in routine clinical practice this would be impractical. It is possible that our patients were therefore less tolerant of the novel route of administration and that exploration of the tablet with the tongue resulted in repeated minor displacements of the tablet in the first few minutes before firm adherence, and in increased solubilisation into subsequently swallowed saliva. Both effects would reduce bioavailability. Clearly, kinetic data directly applicable to our own study are required to substantiate these arguments and this work is being done.

The greater bioavailability of buccal than of intramuscular morphine shown by other workers[8,9] is concentrated in a slower plasma decay curve so that, if this is applicable to the use of buccal morphine as a premedication, then the tablet might be expected to make a greater con-

Table 5. Double-blind study. Patient preferences

	Number of patients		
	Active tablet		Active injection
	$n = 20$*		$n = 24$
Tablet acceptable	15 (75.0%)		21 (87.5%)
Injection acceptable	18 (90.0%)		18 (75.0%)
Prefer tablet	6 (30.0%)	$p < 0.01$	16 (66.7%)
Prefer injection	12 (60.0%)	$p < 0.02$	5 (20.8%)
No preference	2 (10.0%)		3 (12.5%)

*No data on two patients.

tribution to per- and postoperative analgesia than the equivalent dose of intramuscular morphine and so predispose the patient to more stable anaesthesia and greater comfort in recovery. However, such a potential benefit would not accrue where the tablet was prematurely removed; this occurred in our studies on several occasions, at reversal of anaesthesia in association with increased salivation and the use of suction apparatus and also on the ward postoperatively, when tablet residues were rejected by a few patients because of an unpleasant taste.

Concerning unwanted effects, the most obvious difference between the two groups of the double-blind study was the incidence of complaints about taste postoperatively (Table 4). This complaint was made by 18 patients (81.8%) in the active tablet group (cf. 50% in the pilot study), but by only two patients (8.3%) in the active injection group. The corresponding pre-operative figures are four patients (18.2%) in the active tablet group (cf. 20.8% in the pilot study) and no patients in the active injection group. These data indicate that there is a noticeable taste associated with the use of buccal morphine as a premedicant drug, which most patients who complained of it described as bitter. The simultaneous finding that there was no notable incidence of taste in the active injection, dummy tablet group means that it will be difficult for us to conduct any purportedly 'blind' trial in the future.

The incidence of taste associated with the use of buccal morphine in our investigations contrasts sharply with the observations of Bell *et al.*[9] who recorded only one complaint of a bitter taste. The explanation may lie in the differing circumstances of use of buccal morphine in our respective areas of investigation. Thus, it is possible that the taste of the tablet was accumulating in our patients pre- and peroperatively whilst, in a population of patients in whom the tablet was being used for postoperative pain relief, such accumulation might not occur due to the use of mouthwashes and sips of water. In spite of the often bitter taste, the majority of patients (83.3% and 75% in the pilot and double-blind studies respectively) who received buccal morphine said it was an acceptable tablet (Tables 3 and 5), although two patients found it sufficiently unpleasant to request removal of the tablet prior to induction of anaesthesia. However, when each patient in the double-blind study was asked to express a preference for either the tablet or the injection given alone (Table 5), the majority of patients in the active tablet group preferred the injection, whilst the tablet was the preferred route of administration in the active injection group. This would seem to be attributable to the differing experiences of tablet taste in the two groups.

There was nothing remarkable about the nature or incidence of other unwanted effects in either group. No mucosal abnormalities attributable to the administration of buccal morphine were seen in either study. Reliability of tablet adherence was notable throughout our investigations, except for the one patient in the pilot study who was withdrawn. The secure attachment of the tablet ensured that there was no aspiration risk peri-operatively. That this is so may always be confirmed by the anaesthetist prior to induction.

No effort was made to standardise patients, operation or anaesthetic technique, so no conclusions may be drawn regarding the peri-operative analgesic contribution of the premedications.

This work has shown that, in terms of anxiolysis and reduction of wakefulness, buccal morphine 10 mg may be safely and effectively administered as premedication, but that an equivalent dose of intramuscular morphine sulphate is more effective.

Acknowledgments

We would like to thank Dr A.A. Goldberg and Dr D.G. Parsons of Pharmax for their helpful discussions and support during the course of these studies. We would also like to thank Mr J.M. Brudenell, Mr H.E. Berry, Mr L.T. Cotton and Professor V.V. Kakkar for permission to include their patients in our investigations.

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Anaesthesia, 1986, Volume 41, pages 1112–1115

Distribution of evoked paraesthesiae and effectiveness of bra plexus block

B. E. SMITH

Summary

The distribution of paraesthesiae evoked by a low power nerve stimulator during performa supraclavicular brachial plexus block was studied in 120 patients. Evoked paraesthesiae in the distr of the median nerve was associated with a significant improvement in effectiveness of the bloc compared with evoked paraesthesiae in the ulnar and radial distributions. A possible explanation finding is proposed.

Key words

Anaesthetic techniques, regional; brachial plexus.
Equipment; nerve stimulators.

When a supraclavicular brachial plexus block is performed paraesthesiae are usually sought as an aid to accurate placement of the needle tip within the plexus.[1,2] Failure to elicit paraesthesiae is associated with an increase in the failure rate to 15%.[3] This study was undertaken to investigate the clinical impression that failure of the block was less likely if paraesthesiae were produced in the distribution of the median nerve rather than in the distribution of the radial and ulnar nerves.

Methods

Studies were carried out in 120 adult patients presenting for surgery under brachial plexus block. Formal consent was obtained and all patients were premedicated with lorazepam 2 mg orally approximately 2 hours pre-operatively.

Supraclavicular block was performed using the approach described by Ball,[4] using a low nerve stimulator (see Appendix) to aid l of the plexus. An uninsulated short be gauge needle was used in all cases. The was introduced to a depth of approximatel and the active electrode of the stimulator a to the needle by means of a small crocod The output power of the stimulator was gr increased until the patient could just perc stimulator pulses. The output power was this level and the needle advanced towa plexus.

Patients were allocated at random to three groups. In group 1, the needle positi adjusted until paraesthesiae were produce distribution of the median nerve, that is, palm of the hand and the middle finger. In 2 and 3 paraesthesiae were sought in the d tion of the ulnar and radial nerves respe

Following negative aspiration tests, a 2-

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dose of the local anaesthetic agent was injected as recommended by Raj.[5] If the perceived strength of the stimulator pulses diminished within 30 seconds, the full dose of local anaesthetic solution was injected over the following 30 seconds, using the immobile needle technique. The agent used consisted of a mixture of equal parts of 1% prilocaine and 0.5% bupivacaine without adrenaline, at a dosage of 0.5 ml/kg. This dosage was chosen in order to produce a sufficiently large volume of solution to fill the brachial plexus while remaining within the toxic limits of components of the mixture, both individually and in combination.

The block was assessed on the basis of analgesia to pinprick in all the nerve territories of the arm. Testing was performed after 15 minutes and again at 30 and 45 minutes for those blocks not effective on first testing. Any block not effective at 45 minutes was deemed to have failed and alternative anaesthetic techniques were employed.

Results

The number of blocks performed and the clinical outcome are summarised in Table 1. The greater proportion of effective blocks in group 1 in comparison to groups 2 and 3 combined is statistically significant ($p < 0.05$, Chi square test).

Failed blocks

Group 1. Three blocks in group 1 were deemed to have failed. One case resulted in no sensory loss whatever, while two blocks failed to produce analgesia in the distribution of the lateral cutaneous nerve of the forearm.

Group 2. Ten of the 42 blocks in this group were unsuccessful. Of these, two blocks showed no sensory loss whatever, four failed to produce satisfactory analgesia in the radial nerve territory, two failed to block the lateral cutaneous nerve of the forearm, whilst the remaining two produced generally 'patchy' analgesia.

Group 3. Seven of 37 blocks in this group were unsatisfactory. In one block no sensory loss occurrred, five cases had inadequate analgesia of the ulnar territory and one produced patchy analgesia generally.

Table 1. Effectiveness of supraclavicular block in each group. The higher incidence of effective blocks in group 1 in comparison to groups 2 and 3 combined is statistically signficant; $p < 0.05$ (Chi squared test)

	Total number of blocks	Number effective (%)
Group 1 (median)	41	38 (93)
Group 2 (ulnar)	42	32 (76)
Group 3 (radial)	37	30 (81)

Complications

There were no systemic adverse effects in any patient and, in particular, there was no clinical evidence of pneumothorax. Six patients had paroxysms of coughing during performance of the block, but chest X ray revealed no pneumothorax. No cases of postanaesthetic neuritis occurred.

Discussion

The clinical impression that a higher success rate results if paraesthesiae during supraclavicular brachial plexus block are evoked in the distribution of the median nerve has been confirmed by the results of this study. A close inspection of the anatomy of the brachial plexus in the clavicular region provides a possible explanation for this finding. The brachial plexus is formed by the fusion of the anterior rami of $C_{5,6,7,8}$ and T_1, with a variable contribution from C_4 and T_2 (Fig. 1). The nerves emerge in the paravertebral gutter and lie between the anterior and middle scalene muscles. The roots unite to form the principal trunks of the plexus in the posterior triangle of the neck. Just above or behind the clavicle the trunks split into the posterior and anterior divisions of the plexus. These unite to produce the cords of the plexus at, or just lateral to, the outer border of the first rib,[6-9] which then pass into the axilla along with the axillary artery.

In the classical supraclavicular approach,[10] the skin is pierced 2 cm above the midpoint of the clavicle and the needle directed in the familiar downwards, inwards and backwards direction, pointing approximately at the body of T_3. The plexus is generally encountered at a depth of about 2–4 cm depending on the adiposity of the patient. In this case, the needle tip will be lying

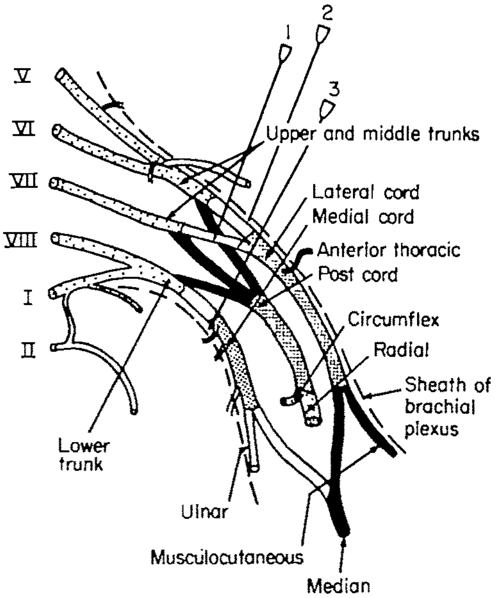

Fig. 1. Diagram of brachial plexus showing needle positions for paraesthesiae in the three separate territories. 1, median; 2, radial; 3, ulnar territories.

close to the point of origin of the divisions of the plexus from the trunks. The local anaesthetic agent would, therefore, be deposited both in the regions of the trunks and the divisions.

Ball's[4] approach is somewhat different however. The point of skin puncture is immediately above the clavicle, lateral to the subclavian artery. The needle is then directed 'vertically downwards' (i.e. horizontally with the patient lying flat) and 'inwards'. The traditional 'backwards' is not used. This results in the needle 'aiming' at the outer border of the first rib, lateral to the subclavian artery. A needle introduced in this direction would meet the brachial plexus at a point just caudal to the inferior border of the clavicle, and approximately 1–2 cm distal to the point of contact of the plexus when using the traditional approach. In this situation, the needle tip will lie in the region of the divisions of the brachial plexus, proximal to the formation of the cords.

Paraesthesiae in the median nerve territory may represent stimulation of the anterior division of the middle trunk with referral of the paraesthesiae to the C_7 dermatome, consistent with the exclusive C_7 origin of the middle trunk. Placement of the needle tip in this position (position 1, Fig. 1) would ensure a more central deposition of the local anaesthetic agent within the sheath of the plexus. This would reduce the likelihood of the anaesthetic solution being deposited outside the plexus following any inadvertent movement of the needle tip. In contrast, if the needle tip lies in position 2 or 3 in Fig. 1, then even slight movement of the needle tip could result in part or all of the anaesthetic solution being deposited outside the sheath of the plexus. Positions 2 and 3 would produce paraesthesiae in the C_{5-6} and C_8–T_1 dermatomes respectively, stimulating the radial and ulnar nerve territories.

The supraclavicular approach to the brachial plexus is a relatively simple technique yet still carries an appreciable failure rate of between 10 and 20%.[11,12] In this series the overall failure rate was 21% in groups 2 and 3 combined, but only 7% in group 1.

Analysis of the blocks which failed in each group suggests that impaired spread of anaesthetic solution was chiefly responsible. In view of the relatively large volumes used (0.5 ml/kg) this may indicate that a significant fraction of the dose was deposited outside the sheath of the brachial plexus. The absence of any demonstrable sensory loss in four cases would suggest that the total dose of anaesthetic was deposited outside the sheath in these cases.

It is possible, however, that the nerve stimulator used could have produced paraesthesiae without the needle tip lying within the sheath of the plexus. This could occur with too deep a penetration, with stimulation resulting from the shaft of the needle, or with insufficient penetration of the needle as the nerve may be stimulated at a distance of 2–3 mm from the needle tip at the stimulating voltages used (3–6 V).[5] In the latter case, the 2 ml test dose could give a false positive result if the plexus were displaced away from the needle tip by the test dose.

Positioning of the needle tip to produce maximal strength of perception of the pulses may reduce this possibility.[5] It is therefore suggested that paraesthesiae in the C_7 dermatome should be actively sought when performing a supraclavicular block. If a low power nerve stimulator is used, then in addition to the use of the 2-ml test dose, the needle tip should be positioned to produce maximal strength of perception of the stimulator pulses.

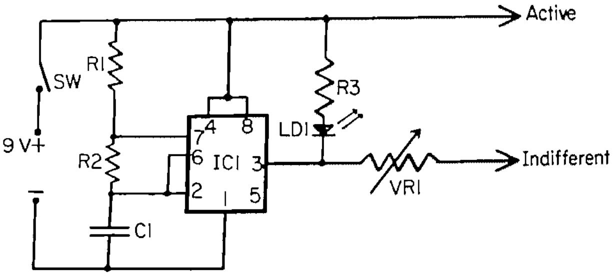

Fig. 2. Circuit diagram of the stimulator. IC1, ICM 7555; R1, 10M0; R2, 22KO; R3, 470; C1, 100 n; VR1, 10KO; LD1, RS 586–481; SW, RS336–624.

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Appendix

The stimulator used in this study is a purpose designed, battery operated solid state pulse generator. The circuit diagram is shown in Fig. 2. The frequency of the pulses is governed by the combined values of R1 and R2. The pulse duration is governed by R2 alone. With the values shown, the frequency will be approximately 1.6 Hz (100 pulses/minute) and the pulse duration 1.4 mS. The output pulse at pin 3 will be of rectangular wave type. The pulse power is controlled by the variable resistor VR1. For a 1 k ohm dummy load this gives a range of 0.4–8 volts and a current flow of 0.4–8 mA. The light emitting diode LD1 gives a visual indication of the stimulator pulse. The mean current consumption of the unit is only about 200 uA which results in a battery life only slightly below shelf life.

All the components used are readily available from commercial stockists and the complete unit can be built for around £7.00. The present model was built on a printed circuit board but Veroboard® would be quite satisfactory.

Further details may be obtained from the author on request.

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Potentiation of epidural opioids with epidural droperidol

A one year retrospective study

V. BACH, P. CARL, O. RAVLO, M. E. CRAWFORD AND M. WERNER

Summary

During a period of one year, 119 patients with chronic pain received injections of opioids via a cat inserted in the lumbar epidural space. Twenty-three patients (19%) showed evidence of toleranc were given droperidol 1.25–5.0 mg epidurally. In 20 patients in this study, there was a significant redu in the number of epidural opioid injections. Six patients complained of excessive sedation, which disapp when the dose of droperidol was reduced, although this did not affect the analgesia. One patient giv accidental overdose of droperidol developed reversible Parkinsonism. It is concluded that epidura ministration of the dopamine antagonist droperidol may be beneficial as supplementary medicati epidural opioids when tolerance develops.

Key words

Anaesthetic techniques, regional; epidural.
Hypnotics, butyrophenones; droperidol.

During the past decade the use of epidural opioids for treatment of chronic as well as postoperative pain has increased. Nevertheless, long term treatment studies have illustrated that supplementary medication is sometimes necessary.[1] Thus, local anaesthetics and phenol have been applied epidurally and intrathecally, systemic sedatives and hypnotics administered and other analgesics injected parenterally.

During the past year, we have administered droperidol epidurally, in order to potentiate epidural opioids at a segmental level. The treatment upon which our results are based, originate from several experimental studies.[2-4]

Methods

The study comprised 20 patients suffering chronic pain who were receiving treatmen epidural opioids for more than 7 days, eit hospital or as outpatients. The narcotic gesics used were either morphine chloride 0.8 mg/ml or buprenorphine 0.03 mg/ml injected neuroleptic agent was drop 2.5 mg/ml, a solution without preservativ with a pH value similar to that of mor chloride (3.5; pKa 7.64). Epidural droperid used in the following circumstances: incr dose of epidural opioids had proven ineffec

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sudden increase in demand for epidural opioids, that is suspected development of tolerance; a sudden loss of effectiveness of epidural opioids. The position of the tip of the epidural catheter was tested either by radiography or by instillation of local anaesthetics.

The effectiveness of droperidol was assessed by looking at the total daily dose of epidural opioid, the number of daily injections of epidural opioids and by using a 0–4 pain relief scale (0, no relief, 1, slight relief, 2, moderate relief, 3, good relief and 4 complete relief). Any side effects were noted. The statistics used were nonparametric; Wilcoxon's test was used for paired differences and Mann Whitney U test for the comparison of two groups.

Results

During a period of one year (March 1983–March 1984) 119 patients suffering from chronic pain were subjected to long term treatment with epidural opioids (more than 7 days) injected via a catheter in the lumbar region. In 23 of these cases (19.3%), epidural droperidol was added. Three patients were not included in assessment of the results: one child, in whom scoring pain relief proved impossible, one adult with rapidly spreading malignant disease and one adult in whom the epidural opioids were discontinued.

The diagnoses of the 20 patients included are shown in Table 1. Seventeen patients (85%) suffered from malignant diseases and three patients (15%) from benign diseases (two fractured hips and one post laminectomy back pain). The median age was 64.5 years (range 32–87 years). Fifteen patients (75%) received morphine chloride and five (25%) buprenorphine. The median daily doses of epidural opioids are shown in Table 2.

Table 1. Main diagnoses of 20 patients treated with droperidol epidurally

3 Benign	
17 Malignant	
Lung and breast	3
Gastrointestinal	3
Urological	5
Gynaecological	3
Other	3

Prior to injection of droperidol, the daily dose of morphine chloride totalled 30 mg (range 12–32 mg) and of buprenorphine 1.35 mg (range 0.6–5.4 mg). Following epidural droperidol, the daily doses were reduced to 20 mg (range 4–40 mg) and 1.35 mg (range 0.6–1.35 mg) respectively. The values for morphine chloride were significantly different ($p < 0.05$). The number of daily dosages of morphine was also reduced significantly (Table 3), from 4 (range 2–5) to 3 (range 2–4) per day ($p < 0.05$) following epidural droperidol. No differences could be detected in the buprenorphine group, but when the groups are combined, the difference is significant. Pain relief scores increased significantly in both groups, as well as when combined (Table 4). The median values were 2 before and 4 after the administration of droperidol ($p < 0.01$). Altogether, 16 out of 20 patients showed an improved pain relief score (80%). The median daily dose of opioid was reduced with ten patients (50%) and the number of daily injections decreased with eight patients (40%).

The median daily dose of droperidol was 2.9 mg (range 1.25–30 mg) administered as 1.9 (range 1–6) injections. These figures are biased by the fact that one of the patients received an accidental daily dose of 30 mg of droperidol. In the case of one patient, a daily dose of 15 mg (3 × 5 mg) was completely ineffective. In all other cases, the usual dosage of droperidol amounted to 1.25–2.5 mg once or twice daily, given immediately prior to the instillation of epidural opioid.

Seven patients experienced unwanted side effects during treatment. Reversible Parkinsonism occurred with the patient who received the

Table. 2. Daily dose (mg) of opioid epidurally

	Number of patients	Median before droperidol	Median after droperidol	Median pair differences	Test for pair differences
Morphine	15 (75%)	30 (18–32)	20 (16–32)	8 (0–12)	$p<0.05$
Buprenorphine	5 (25%)	1.35 (0.6–5.4)	1.35 (0.6–1.35)	0 (0–0)	NS

Brackets represent the first and third quartiles. NS: nonsignificant.

Table 3. Number of daily injections epidurally

	Number of patients	Median before droperidol	Median after droperidol	Median pair differences	Test for pair differences
Morphine	15 (75%)	4 (3–5)	3 (2–4)	0 (1–2)	$p<0.05$
Buprenorphine	5 (25%)	3 (2–6)	3 (2–6)	0 (0–0)	NS
Total	20	3 (3–4)	3 (2–4)	0 (0–1)	$p<0.05$

Brackets represent the first and third quartiles. NS: nonsignificant.

Table 4. Pain relief score (PRS)

	Number of patients	Median before droperidol	Median after droperidol	Median pair differences	Test for pair differences
Morphine	15 (75%)	2 (1–2)	4 (3–4)	2 (1–2)	$p<0.01$ Significant
Buprenorphine	5 (25%)	2 (1–2)	4 (2–4)	2 (0–2)	$p<0.01$ Significant
Total	20	2 (1–2)	4 (3–4)	2 (1–2)	$p<0.01$ Significant

Brackets represent the first and third quartiles.

accidental dose of 30 mg of droperidol daily for several days. The disorder disappeared following treatment with biperiden. Six patients complained of sedation and these patients were receiving an average of 4.7 mg droperidol compared to 2.2 mg in those who did not have any sedation. A reduction in the dose to an average of 2.0 mg resulted in disappearance of this symptom. No other unwanted side effects were recorded. All patients were specifically asked about nausea and vomiting, bladder trouble, pruritus, dizziness, constipation and changes of the mood. There was no evidence of respiratory depression.

To investigate the toxic effect of epidural droperidol, the spinal medulla of a man who had been successfully treated with epidural droperidol in combination with epidural opioid for 4 months was examined at postmortem. No signs of necrosis, inflammation or other structural changes were found.

The pharmacokinetics of epidural droperidol were investigated in a small study comprising three patients. In one patient, we administered 5 mg of droperidol intravenously and in two patients 1.25 and 2.5 mg epidurally. The results showed some uptake of droperidol into the blood, whereas the drug could not be detected in the cerebrospinal fluid after intravenous administration. The blood concentrations after epidural administration were lower than after intravenous administration. We found no sedative or direct analgesic effect with the epidural doses.

Discussion

Potentiation of enterally/parenterally administered opioids by means of neuroleptic agents is a well known phenomenon. Tulunay and co-workers[5] showed that the use of dopamine receptor blocking agents lowered the ED_{50} of parenteral opioids. Other investigators have demonstrated independent and descending dopaminergic tracts in the spinal medulla.[2,3] Jensen and Smith[6] evaluated the effect of intrathecal dopamine agonists on the tailflick reflex in rats. Dopamine and apomorphine had an inhibitory effect on the response, which seems to be the opposite to our findings, but the effect could only be demonstrated in spinal animals and was not investigated in combination with opioids. The reaction may be different in awake, normal animals, but this has not been investigated. Kim and Stoelting[4] administered droperidol together with morphine intrathecally in normal rats. Addition of droperidol prolonged the duration of intrathecal morphine by 40%. Furthermore, droperidol seemed to inhibit development of tolerance.

A Danish multicentre study revealed that 33% of patients suffering from chronic pain and treated with epidural opioids required supplementary medication. This consisted of analgesics, neuroleptics (8%), and epidural local anaesthetics.[1] In rare cases, it has proven necessary to inject intrathecal phenol. Most of the mentioned combinations produce adverse effects, especially central nervous symptoms.

In treating cancer patients, we find it essential to reduce the incidence of unwanted side effects due to medication as much as possible and also to offer the simplest way of administering this treatment. In our study, three patients with nonmalignant diseases are included, but they were old and in a rather terminal state. In general, we try to avoid droperidol epidurally in patients with nonmalignant disease as the toxic effects are not fully evaluated.

Epidural droperidol seems to potentiate the effects of epidural opioids. In our study 80% of the patients had significantly better scores following its use. The median daily dose and median number of daily injections were reduced significantly in the morphine group, but not in the small buprenorphine group. It should be noted that in no patient was there a reduction in the degree of pain relief after administration of droperidol.

The only frequent side effect was sedation (six patients), a symptom that was eliminated following reduction in the dose of droperidol but without affecting pain relief. A comparison of the dose range indicates that the initial dose of droperidol must be low and adjusted on an individual basis, keeping in mind that major dosages may elicit catalepsy, as in the case of reversible Parkinsonism in our study.

In cancer patients, nausea and vomiting are regular complaints. We had hoped to see the antiemetic effect of droperidol prove useful in our patients, but, surprisingly, there were no cases of nausea prior to droperidol administration.

The importance of central and placebo effects remains unknown in this retrospective study and an analgesic effect of droperidol remains to be clarified in a double-blind placebo study. Likewise, the target zone of droperidol (segmental ?) must be evaluated in pharmacokinetic studies. Our preliminary pharmacokinetic study revealed that the effect of droperidol cannot be explained solely by uptake into the blood, because of the relatively low concentrations. However, some central nervous effects must be expected.

In conclusion, we believe that droperidol, injected epidurally, may potentiate epidural opioids without increasing the incidence of unwanted side effects. Whenever the effect of epidural opioid is inadequate or tolerance develops, droperidol might be the supplementary drug of choice. The effective daily dosage of droperidol averages 2.5 mg/day distributed as two injections. It is advisable to start at approximately 1.25 mg/day due to individual variation and risk of sedation.

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CASE REPORT

Narcotic-induced choledochoduodenal sphincter spasm reversed by naloxone

A case report and review

K. J. BIRD

Summary

A case report of biliary colic induced by narcotic premedication and reversed by naloxone administration is described and the literature reviewed.

Key words

Antagonists, narcotic; naloxone.
Analgesics, narcotic; papaveretum.

Narcotic analgesics are known to cause spasm of the choledochoduodenal sphincter (sphincter of Oddi). This may have two important consequences: upper abdominal pain in the awake patient, or failed passage of contrast medium during operative cholangiography, giving a false impression of distal common bile duct obstruction. Many drugs have been used with varying success to prevent or reverse this spasm. A patient is described who presented for non-biliary tract surgery and who, following premedication with papaveretum and hyoscine, experienced severe biliary colic which dramatically resolved on administration of naloxone.

Case history

A fit 27-year-old female with five children presented for laparoscopic sterilisation. Apart from cholecystectomy at the age of 19 years, her past medical history was uneventful. Fifteen minutes after premedication with papaveretum 15 mg and hyoscine 0.3 mg, she complained of severe colicky abdominal pain which she likened to that she experienced before her cholecystectomy. For 15 minutes the author observed a typical severe biliary colic whilst awaiting the arrival of naloxone. At the height of a colic 0.2 mg of naloxone was given intravenously and was followed by an almost immediate cessation of the pain. A further 0.2 mg was given intramuscularly and there was no recurrence.

The next day, after a premedication of pethidine 50 mg and promethazine 25 mg, she had an uneventful laparoscopic sterilisation. Follow-up investigations included normal liver function tests and a normal ultrasound of the biliary system. Surgical opinion was that the most likely explanation of the episode was a drug-induced biliary spasm.

Discussion

Both naturally occurring and synthetic narcotic analgesic drugs have been shown to increase intrabiliary pressure due to choledochoduodenal

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buccal formulation is somewhat more bioavailable.[8,9] A pilot study was undertaken as an initial assessment of the potential of buccal morphine as premedication. As an examination of a new formulation, this was conducted as an open study, but favourable results indicated that a double-blind comparison with an established route of administration should be made. Both studies were conducted with the approval of the hospital ethical committee.

Methods

Fifty patients, ASA grade 1 or 2 who were not being treated with narcotic analgesics or other sedative or anxiolytic drugs and scheduled for elective surgery, were admitted to the study. On admission, each patient was assigned a trial number in a random fashion ensuring the receipt, at premedication, of the contents of an identically numbered packet. Each packet held a buccal tablet and an ampoule, the contents of which were for intramuscular injection. Within a packet, either the buccal tablet contained 10 mg morphine base, in which case the injection was placebo, or the buccal tablet was placebo, in which case the injection consisted of 13.5 mg morphine sulphate. In the pilot study, 25 patients fulfilling the above admission criteria were premedicated with buccal morphine 10 mg.

On the day prior to surgery each patient's informed, written consent was obtained, the use of linear analogue scales explained and a record made of patient height, weight, baseline blood pressure and heart rate. On the day of surgery, 90 minutes before the estimated time of induction of anaesthesia, measurements and assessments were made as follows: blood pressure, heart rate and respiratory rate (pilot study only); the patient also indicated levels of anxiety and wakefulness on two independently presented linear analogue scales, each consisting of a 10-cm horizontal straight line, marked at each end 'no anxiety', 'extremely anxious' and 'extremely drowsy', 'wide awake', respectively.

Premedication was administered after completion of these observations, which were subsequently repeated by the same observer at 15, 30, 60 minutes and in the anaesthetic room at 90 minutes. Sleeping patients were not disturbed. Patient acceptability was assessed preoperatively by recording any spontaneous observations made by the patient concerning the tablet or injection and, unless the patient was asleep, by asking, 'Does the treatment suit you? Has it upset you in any way?'. Any unwanted effects were noted. Patients were questioned directly about nausea or vomiting.

At induction of anaesthesia, patients were examined to confirm the continued presence of the tablet. Details of the anaesthetic and patient vital signs peroperatively were recorded, including the respiratory rate of spontaneously breathing patients, further opioid administration and time to awakening following discontinuation of the anaesthetic. Anaesthetists were asked to record any complications encountered or observations they wished to make concerning the anaesthetic course.

Postoperatively, recordings were made of patient vital signs in recovery and on the ward, the incidence of nausea and vomiting and the time to first administration of postoperative analgesia. On the first postoperative day, a visit was made to re-assess the acceptability to the patient of the two routes of drug administration, to elicit any preference for one or other route alone, to record any unwanted effects and to examine the buccal mucosa.

A paired t-test was used in both studies to detect any statistically significant intragroup changes from baseline values of vital signs, anxiety and wakefulness scores during the premedication period. In the double-blind study an unpaired t-test was used to detect any statistically significant intergroup differences in anxiety and wakefulness scores at each assessment.

Results

Demographic data

From the initial group of 25 patients in the pilot study, one female was withdrawn at 60 minutes due to displacement of the tablet. Data on three patients in the double-blind study were lost. The demographic data relating to the two studies are shown in Tables 1 and 2 respectively.

Table 1. Pilot study demographic data (mean, range)

Age (years)	43 (18– 76)
Weight (kg)	68 (49–104)
Height (cm)	170 (150–188)

Table 2. Double-blind study demographic data

	Active tablet ($n = 22$)	Active injection ($n = 25$)
Patient details		
Age (years, mean SEM)	40.04 (2.34)	45.17 (2.85)
Weight (kg, mean SEM)	66.02 (1.67)	65.98 (2.41)
Height (m, mean SEM)	1.67 (0.02)	1.67 (0.02)
Male: Female	5:17	7:18
Operation details		
Hysterectomy	5	5
Tubal surgery	2	3
Colposuspension	2	3
Laparoscopy	1	2
Cholecystectomy	3	1
Varicose veins	4	3
Haemorrhoidectomy	1	1
Herniorrhaphy	1	2
Other	3	5

Vital signs

There were no statistically significant changes detected in blood pressure, heart rate or respiratory rate over the premedication period. In addition to the stability of vital signs shown statistically for the group, it was also noted that there were no clinically significant changes in individual patients. In particular, there was no respiratory depression as assessed by respiratory rate.

Anxiety

For each assessment, group mean linear analogue anxiety scores were plotted against time (pilot study, Fig. 1; double-blind study, Fig. 2). In the pilot study, statistically significant reductions in linear analogue anxiety scores were detected at 15, 30 and 60 minutes, but not in the anaesthetic room, by comparison with baseline level. In the double-blind study, statistically significant reductions in anxiety were detected at 30 minutes in the active tablet group and at 15, 30 and 60 minutes in the active injection group. There was a significantly greater anxiolytic effect in the active injection group at 15 minutes and in the anaesthetic room, although in neither group was there a significant difference between baseline and anaesthetic room anxiety levels.

Wakefulness

Data were processed in the same way as for anxiety data (pilot study, Fig. 3; double-blind study, Fig. 4). In both studies, and in all groups, statistically significant decreases in linear analogue wakefulness scores, by comparison with baseline, were detected at all assessment times. In the double-blind study, the reduction in wakefulness was significantly more marked at all assessments in the active injection group.

Peroperative course

There were no untoward complications peroperatively. The buccal tablet was found to pose no aspiration risk. There was no undue respiratory depression in spontaneously breathing patients. Two anaesthetists commented upon excessive salivation at reversal. Suction at this stage occasionally removed buccal tablet residue. Time to awakening was not clinically prolonged.

Patient acceptability

Data relating to the incidence and nature of unwanted effects peri-operatively are shown in Tables 3 and 4 for the pilot and double-blind studies respectively. Table 5 (double-blind study) shows the acceptability to patients of the two routes of administration and their preferences for one or other route.

Discussion

The advent of a buccal formulation of morphine requires that its potential usefulness in anaesthetic practice be assessed. An initial comparison of buccal with intramuscular morphine in post-

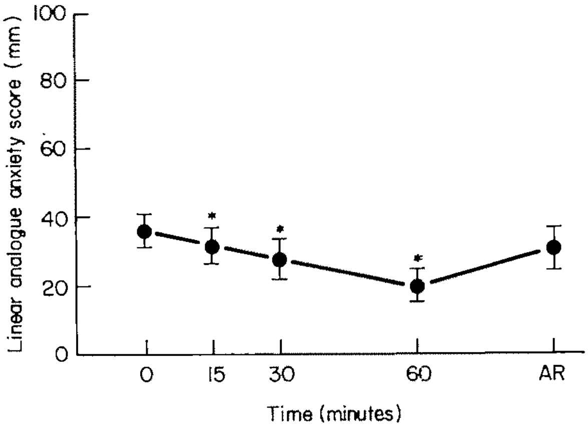

Fig. 1. Pilot study. Changes in anxiety as shown by linear analogue scores (mean, SEM). AR, Anaesthetic room (*c*. 90 minutes); *, $p < 0.05$ (paired *t*-test, $n = 24$).

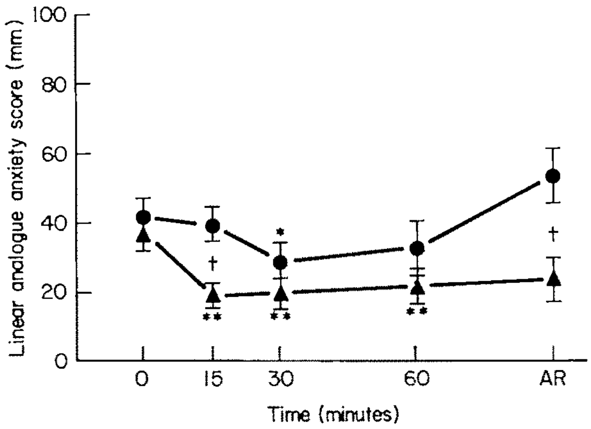

Fig. 2. Double-blind study. Changes in anxiety as shown by linear analogue scores (mean, SEM). AR, Anaesthetic room (*c*. 90 minute); ●, active tablet group ($n = 22$); ▲, active injection group ($n = 25$); *, $p < 0.05$; **$p < 0.01$, (paired *t*-test intragroup); †$p < 0.05$ (unpaired *t*-test intergroup).

Table 3. Pilot study. Unwanted effects and acceptability ($n = 24$)

Pre-operative	
Unwanted effects	7 (29.2%)
Nausea	0 (0.0)
Vomiting	0 (0.0)
Taste	5 (20.8%)
Headache	2 (8.3%)
Postoperative	
Nausea, vomiting	9 (37.5%)
Taste	12 (50.0%)
Mucosal abnormalities	0 (0.0)
Tablet acceptable	20 (83.3%)

operative pain control has been made by Bell *et al.*[9] Whilst more specifically anxiolytic drugs than morphine are available and potent, rapidly acting analgesics may be administered intravenously at induction of anaesthesia, it is still common practice to premedicate patients with opioids.

The difficulties inherent in the quantification of the subjective experience of anxiety have long been appreciated and the problem has been reviewed by Norris.[10] Wassenaar *et al.*[11] reported the use of the Multiple Affect Adjective Check

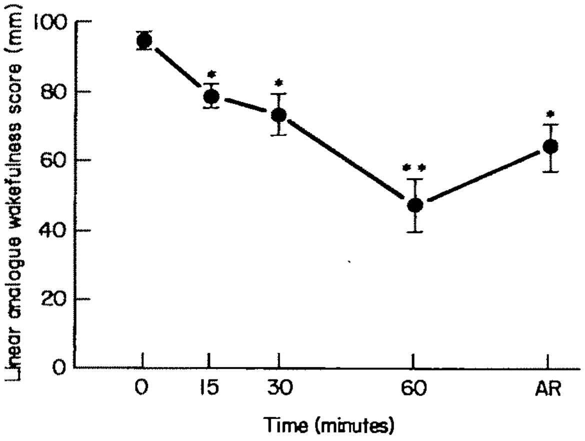

Fig. 3. Pilot study. Changes in wakefulness as shown by linear analogue score (mean, SEM). AR, Anaesthetic room (c. 90 minutes); *p < 0.05; **, p < 0.001 (paired t-test, $n = 24$).

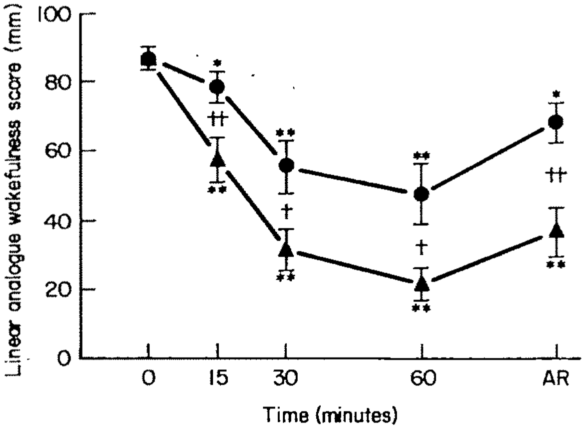

Fig. 4. Double-blind study. Changes in wakefulness as shown by linear analgoue score (mean, SEM). AR, Anaesthetic room (c. 90 minutes; ●, active tablet group ($n = 22$); ▲, active injection group ($n = 25$); *, $p < 0.05$; **$p < 0.001$ (paired t-test intragroup); †, $p < 0.05$; ††$p < 0.001$ (unpaired t-test intergroup).

List (MAACL) as devised by Zuckerman[12] in the assessment of pre-operative anxiety, and recently Elliott *et al.*[13] found a strong correlation between anxiety scores as measured by MAACL and linear analogue scores. Fell *et al.*,[14] in assessing the value of plasma catecholamine concentration measurement as an objective index of anxiety, have produced data which support the use of the linear analogue score as a measure of anxiety in the pre-operative patient.

The linear analogue score method was used in these studies because of the simplicity of the technique, coupled with the minimum of disturbance to the patient. In both studies, the linear analogue scores showed progressive reduction in anxiety and wakefulness following administration of buccal morphine. Statistical analysis of the scores showed these reductions to be significant. However, the double-blind study showed that intramuscular morphine appeared to have a more profound effect of quicker onset by comparison with buccal morphine and the increase in anxiety

Table 4. Double-blind study. Unwanted effects

	Number of patients	
	Active tablet	Active injection
	$n = 22$	$n = 25$
Pre-operative		
Unwanted effects	10 (45.4%)	7 (28.0%)
Nausea	1 (4.5%)	4 (16.0%)
Vomiting	0 (0.0%)	1 (4.0%)
Taste	4 (18.2%)	0 (0.0%)
Headache	4 (18.2%)	2 (8.0%)
Painful injection site	4 (18.2%)	1 (4.0%)
Postoperative	$n = 22$	$n = 24$*
Nausea	16 (72.7%)	13 (54.2%)
Vomiting	6 (27.3%)	11 (45.8%)
Taste	18 (81.8%) $p<0.001$	2 (8.3%)
Mucosal abnormality	0 (0.0%)	0 (0.0)

*One patient discharged home prior to postoperative assessment.

and wakefulness observed in the anaesthetic room was less marked in the active injection group.

The variability of response to the active tablet between patients was marked; some patients were apparently minimally affected whilst others were asleep at 60 minutes. Some of this variability may be ascribed to differing sensitivity of individuals to opioids, but it is likely that there was also variable rate of absorption of the drug.

Greatest depression of anxiety and wakefulness was found to occur at 60 minutes, which parallels the time to peak plasma morphine levels as measured in a kinetic study,[8] but our result must contain a methodological component in that the assessment subsequent to that at 60 minutes took place in the anaesthetic room after a disturbing journey through the hospital corridors, which, one assumes, can only increase anxiety and wakefulness.

Although any relationship between plasma levels of morphine and central nervous system effects may not be simple in view of the poor lipid solubility of the drug, the difference between the performances of the buccal and intramuscular preparations may find some explanation on the basis of the pharmacokinetic data available from the work of Bell *et al.*[9] They found that the plasma morphine level rose more quickly and to a higher peak value at about one hour after intramuscular administration, whereas after buccal administration a lower peak was achieved at between 1 and 2 hours. Such kinetic differences occurring over the 90 minute premedication period of our study could well be expected to produce disparate degrees of clinical effect.

In addition, there are three factors to consider which may have impaired the performance of the tablet in our investigation. Firstly, any tendency to dryness of the mouth due to pre-operative anxiety may decrease the early bioavailability of buccal morphine because of retarded adherence and solubilisation at the mucosa. Secondly, Bell *et al.*[9] report that 'the tablets were usually moistened (to facilitate their adherence to the mucosa)'. This manoeuvre was not employed in our studies. Thirdly, they used placebo buccal tablets to familiarise their patients with the route of administration prior to the study, which we omitted on the basis that in routine clinical practice this would be impractical. It is possible that our patients were therefore less tolerant of the novel route of administration and that exploration of the tablet with the tongue resulted in repeated minor displacements of the tablet in the first few minutes before firm adherence, and in increased solubilisation into subsequently swallowed saliva. Both effects would reduce bioavailability. Clearly, kinetic data directly applicable to our own study are required to substantiate these arguments and this work is being done.

The greater bioavailability of buccal than of intramuscular morphine shown by other workers[8,9] is concentrated in a slower plasma decay curve so that, if this is applicable to the use of buccal morphine as a premedication, then the tablet might be expected to make a greater con-

Table 5. Double-blind study. Patient preferences

	Number of patients		
	Active tablet		Active injection
	$n = 20$*		$n = 24$
Tablet acceptable	15 (75.0%)		21 (87.5%)
Injection acceptable	18 (90.0%)		18 (75.0%)
Prefer tablet	6 (30.0%)	$p<0.01$	16 (66.7%)
Prefer injection	12 (60.0%)	$p<0.02$	5 (20.8%)
No preference	2 (10.0%)		3 (12.5%)

*No data on two patients.

tribution to per- and postoperative analgesia than the equivalent dose of intramuscular morphine and so predispose the patient to more stable anaesthesia and greater comfort in recovery. However, such a potential benefit would not accrue where the tablet was prematurely removed; this occurred in our studies on several occasions, at reversal of anaesthesia in association with increased salivation and the use of suction apparatus and also on the ward postoperatively, when tablet residues were rejected by a few patients because of an unpleasant taste.

Concerning unwanted effects, the most obvious difference between the two groups of the double-blind study was the incidence of complaints about taste postoperatively (Table 4). This complaint was made by 18 patients (81.8%) in the active tablet group (cf. 50% in the pilot study), but by only two patients (8.3%) in the active injection group. The corresponding pre-operative figures are four patients (18.2%) in the active tablet group (cf. 20.8% in the pilot study) and no patients in the active injection group. These data indicate that there is a noticeable taste associated with the use of buccal morphine as a premedicant drug, which most patients who complained of it described as bitter. The simultaneous finding that there was no notable incidence of taste in the active injection, dummy tablet group means that it will be difficult for us to conduct any purportedly 'blind' trial in the future.

The incidence of taste associated with the use of buccal morphine in our investigations contrasts sharply with the observations of Bell *et al.*[9] who recorded only one complaint of a bitter taste. The explanation may lie in the differing circumstances of use of buccal morphine in our respective areas of investigation. Thus, it is possible that the taste of the tablet was accumulating in our patients pre- and peroperatively whilst, in a population of patients in whom the tablet was being used for postoperative pain relief, such accumulation might not occur due to the use of mouthwashes and sips of water. In spite of the often bitter taste, the majority of patients (83.3% and 75% in the pilot and double-blind studies respectively) who received buccal morphine said it was an acceptable tablet (Tables 3 and 5), although two patients found it sufficiently unpleasant to request removal of the tablet prior to induction of anaesthesia. However, when each patient in the double-blind study was asked to express a preference for either the tablet or the injection given alone (Table 5), the majority of patients in the active tablet group preferred the injection, whilst the tablet was the preferred route of administration in the active injection group. This would seem to be attributable to the differing experiences of tablet taste in the two groups.

There was nothing remarkable about the nature or incidence of other unwanted effects in either group. No mucosal abnormalities attributable to the administration of buccal morphine were seen in either study. Reliability of tablet adherence was notable throughout our investigations, except for the one patient in the pilot study who was withdrawn. The secure attachment of the tablet ensured that there was no aspiration risk peri-operatively. That this is so may always be confirmed by the anaesthetist prior to induction.

No effort was made to standardise patients, operation or anaesthetic technique, so no conclusions may be drawn regarding the peri-operative analgesic contribution of the premedications.

This work has shown that, in terms of anxiolysis and reduction of wakefulness, buccal morphine 10 mg may be safely and effectively administered as premedication, but that an equivalent dose of intramuscular morphine sulphate is more effective.

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Anaesthesia, 1986, Volume 41, pages 1112–1115

Distribution of evoked paraesthesiae and effectiveness of bra(plexus block

B. E. SMITH

Summary

The distribution of paraesthesiae evoked by a low power nerve stimulator during performa supraclavicular brachial plexus block was studied in 120 patients. Evoked paraesthesiae in the distri of the median nerve was associated with a significant improvement in effectiveness of the block compared with evoked paraesthesiae in the ulnar and radial distributions. A possible explanation j finding is proposed.

Key words

Anaesthetic techniques, regional; brachial plexus.
Equipment; nerve stimulators.

When a supraclavicular brachial plexus block is performed paraesthesiae are usually sought as an aid to accurate placement of the needle tip within the plexus.[1,2] Failure to elicit paraesthesiae is associated with an increase in the failure rate to 15%.[3] This study was undertaken to investigate the clinical impression that failure of the block was less likely if paraesthesiae were produced in the distribution of the median nerve rather than in the distribution of the radial and ulnar nerves.

Methods

Studies were carried out in 120 adult patients presenting for surgery under brachial plexus block. Formal consent was obtained and all patients were premedicated with lorazepam 2 mg orally approximately 2 hours pre-operatively.

Supraclavicular block was performed using the approach described by Ball,[4] using a low nerve stimulator (see Appendix) to aid lc of the plexus. An uninsulated short be gauge needle was used in all cases. The was introduced to a depth of approximatel and the active electrode of the stimulator at to the needle by means of a small crocodi The output power of the stimulator was gr increased until the patient could just perce stimulator pulses. The output power was f this level and the needle advanced towa plexus.

Patients were allocated at random to three groups. In group 1, the needle positi adjusted until paraesthesiae were produce distribution of the median nerve, that is, palm of the hand and the middle finger. In 2 and 3 paraesthesiae were sought in the di tion of the ulnar and radial nerves respec

Following negative aspiration tests, a 2-

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dose of the local anaesthetic agent was injected as recommended by Raj.[5] If the perceived strength of the stimulator pulses diminished within 30 seconds, the full dose of local anaesthetic solution was injected over the following 30 seconds, using the immobile needle technique. The agent used consisted of a mixture of equal parts of 1% prilocaine and 0.5% bupivacaine without adrenaline, at a dosage of 0.5 ml/kg. This dosage was chosen in order to produce a sufficiently large volume of solution to fill the brachial plexus while remaining within the toxic limits of components of the mixture, both individually and in combination.

The block was assessed on the basis of analgesia to pinprick in all the nerve territories of the arm. Testing was performed after 15 minutes and again at 30 and 45 minutes for those blocks not effective on first testing. Any block not effective at 45 minutes was deemed to have failed and alternative anaesthetic techniques were employed.

Results

The number of blocks performed and the clinical outcome are summarised in Table 1. The greater proportion of effective blocks in group 1 in comparison to groups 2 and 3 combined is statistically significant ($p < 0.05$, Chi square test).

Failed blocks

Group 1. Three blocks in group 1 were deemed to have failed. One case resulted in no sensory loss whatever, while two blocks failed to produce analgesia in the distribution of the lateral cutaneous nerve of the forearm.

Group 2. Ten of the 42 blocks in this group were unsuccessful. Of these, two blocks showed no sensory loss whatever, four failed to produce satisfactory analgesia in the radial nerve territory, two failed to block the lateral cutaneous nerve of the forearm, whilst the remaining two produced generally 'patchy' analgesia.

Group 3. Seven of 37 blocks in this group were unsatisfactory. In one block no sensory loss occurrred, five cases had inadequate analgesia of the ulnar territory and one produced patchy analgesia generally.

Table 1. Effectiveness of supraclavicular block in each group. The higher incidence of effective blocks in group 1 in comparison to groups 2 and 3 combined is statistically signficant; $p < 0.05$ (Chi squared test)

	Total number of blocks	Number effective (%)
Group 1 (median)	41	38 (93)
Group 2 (ulnar)	42	32 (76)
Group 3 (radial)	37	30 (81)

Complications

There were no systemic adverse effects in any patient and, in particular, there was no clinical evidence of pneumothorax. Six patients had paroxysms of coughing during performance of the block, but chest X ray revealed no pneumothorax. No cases of postanaesthetic neuritis occurred.

Discussion

The clinical impression that a higher success rate results if paraesthesiae during supraclavicular brachial plexus block are evoked in the distribution of the median nerve has been confirmed by the results of this study. A close inspection of the anatomy of the brachial plexus in the clavicular region provides a possible explanation for this finding. The brachial plexus is formed by the fusion of the anterior rami of $C_{5,6,7,8}$ and T_1, with a variable contribution from C_4 and T_2 (Fig. 1). The nerves emerge in the paravertebral gutter and lie between the anterior and middle scalene muscles. The roots unite to form the principal trunks of the plexus in the posterior triangle of the neck. Just above or behind the clavicle the trunks split into the posterior and anterior divisions of the plexus. These unite to produce the cords of the plexus at, or just lateral to, the outer border of the first rib,[6-9] which then pass into the axilla along with the axillary artery.

In the classical supraclavicular approach,[10] the skin is pierced 2 cm above the midpoint of the clavicle and the needle directed in the familiar downwards, inwards and backwards direction, pointing approximately at the body of T_3. The plexus is generally encountered at a depth of about 2–4 cm depending on the adiposity of the patient. In this case, the needle tip will be lying

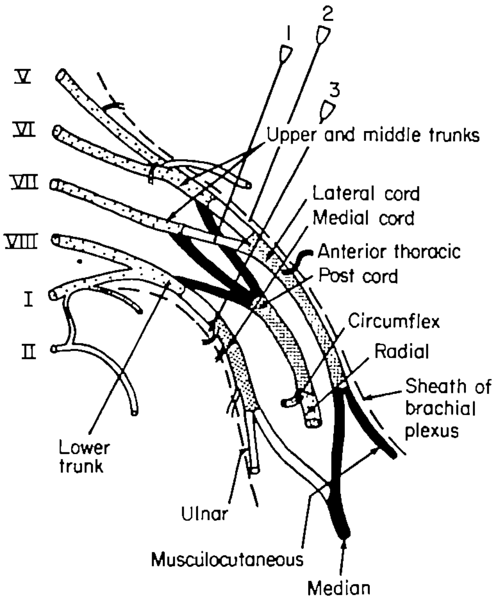

Fig. 1. Diagram of brachial plexus showing needle positions for paraesthesiae in the three separate territories. 1, median; 2, radial; 3, ulnar territories.

close to the point of origin of the divisions of the plexus from the trunks. The local anaesthetic agent would, therefore, be deposited both in the regions of the trunks and the divisions.

Ball's[4] approach is somewhat different however. The point of skin puncture is immediately above the clavicle, lateral to the subclavian artery. The needle is then directed 'vertically downwards' (i.e. horizontally with the patient lying flat) and 'inwards'. The traditional 'backwards' is not used. This results in the needle 'aiming' at the outer border of the first rib, lateral to the subclavian artery. A needle introduced in this direction would meet the brachial plexus at a point just caudal to the inferior border of the clavicle, and approximately 1–2 cm distal to the point of contact of the plexus when using the traditional approach. In this situation, the needle tip will lie in the region of the divisions of the brachial plexus, proximal to the formation of the cords.

Paraesthesiae in the median nerve territory may represent stimulation of the anterior division of the middle trunk with referral of the paraesthesiae to the C_7 dermatome, consistent with the exclusive C_7 origin of the middle trunk. Placement of the needle tip in this position (position 1, Fig. 1) would ensure a more central deposition of the local anaesthetic agent within the sheath of the plexus. This would reduce the likelihood of the anaesthetic solution being deposited outside the plexus following any inadvertent movement of the needle tip. In contrast, if the needle tip lies in position 2 or 3 in Fig. 1, then even slight movement of the needle tip could result in part or all of the anaesthetic solution being deposited outside the sheath of the plexus. Positions 2 and 3 would produce paraesthesiae in the C_{5-6} and C_8–T_1 dermatomes respectively, stimulating the radial and ulnar nerve territories.

The supraclavicular approach to the brachial plexus is a relatively simple technique yet still carries an appreciable failure rate of between 10 and 20%.[11,12] In this series the overall failure rate was 21% in groups 2 and 3 combined, but only 7% in group 1.

Analysis of the blocks which failed in each group suggests that impaired spread of anaesthetic solution was chiefly responsible. In view of the relatively large volumes used (0.5 ml/kg) this may indicate that a significant fraction of the dose was deposited outside the sheath of the brachial plexus. The absence of any demonstrable sensory loss in four cases would suggest that the total dose of anaesthetic was deposited outside the sheath in these cases.

It is possible, however, that the nerve stimulator used could have produced paraesthesiae without the needle tip lying within the sheath of the plexus. This could occur with too deep a penetration, with stimulation resulting from the shaft of the needle, or with insufficient penetration of the needle as the nerve may be stimulated at a distance of 2–3 mm from the needle tip at the stimulating voltages used (3–6 V).[5] In the latter case, the 2 ml test dose could give a false positive result if the plexus were displaced away from the needle tip by the test dose.

Positioning of the needle tip to produce maximal strength of perception of the pulses may reduce this possibility.[5] It is therefore suggested that paraesthesiae in the C_7 dermatome should be actively sought when performing a supraclavicular block. If a low power nerve stimulator is used, then in addition to the use of the 2-ml test dose, the needle tip should be positioned to produce maximal strength of perception of the stimulator pulses.

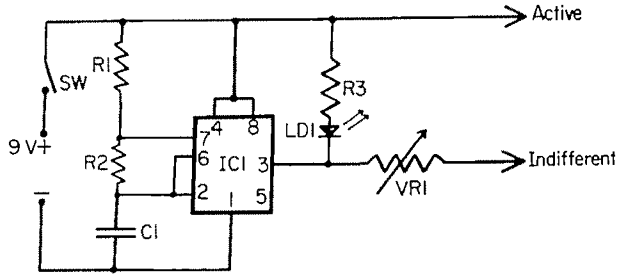

Fig. 2. Circuit diagram of the stimulator. IC1, ICM 7555; R1, 10M0; R2, 22KO; R3, 470; C1, 100 n; VR1, 10KO; LD1, RS 586–481; SW, RS336–624.

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Appendix

The stimulator used in this study is a purpose designed, battery operated solid state pulse generator. The circuit diagram is shown in Fig. 2. The frequency of the pulses is governed by the combined values of R1 and R2. The pulse duration is governed by R2 alone. With the values shown, the frequency will be approximately 1.6 Hz (100 pulses/minute) and the pulse duration 1.4 mS. The output pulse at pin 3 will be of rectangular wave type. The pulse power is controlled by the variable resistor VR1. For a 1 k ohm dummy load this gives a range of 0.4–8 volts and a current flow of 0.4–8 mA. The light emitting diode LD1 gives a visual indication of the stimulator pulse. The mean current consumption of the unit is only about 200 uA which results in a battery life only slightly below shelf life.

All the components used are readily available from commercial stockists and the complete unit can be built for around £7.00. The present model was built on a printed circuit board but Veroboard® would be quite satisfactory.

Further details may be obtained from the author on request.

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Potentiation of epidural opioids with epidural droperidol

A one year retrospective study

V. BACH, P. CARL, O. RAVLO, M. E. CRAWFORD AND M. WERNER

Summary

During a period of one year, 119 patients with chronic pain received injections of opioids via a catheter inserted in the lumbar epidural space. Twenty-three patients (19%) showed evidence of tolerance and were given droperidol 1.25–5.0 mg epidurally. In 20 patients in this study, there was a significant reduction in the number of epidural opioid injections. Six patients complained of excessive sedation, which disappeared when the dose of droperidol was reduced, although this did not affect the analgesia. One patient given an accidental overdose of droperidol developed reversible Parkinsonism. It is concluded that epidural administration of the dopamine antagonist droperidol may be beneficial as supplementary medication to epidural opioids when tolerance develops.

Key words

Anaesthetic techniques, regional; epidural.
Hypnotics, butyrophenones; droperidol.

During the past decade the use of epidural opioids for treatment of chronic as well as postoperative pain has increased. Nevertheless, long term treatment studies have illustrated that supplementary medication is sometimes necessary.[1] Thus, local anaesthetics and phenol have been applied epidurally and intrathecally, systemic sedatives and hypnotics administered and other analgesics injected parenterally.

During the past year, we have administered droperidol epidurally, in order to potentiate epidural opioids at a segmental level. The treatment upon which our results are based, originate from several experimental studies.[2–4]

Methods

The study comprised 20 patients suffering from chronic pain who were receiving treatment with epidural opioids for more than 7 days, either in hospital or as outpatients. The narcotic analgesics used were either morphine chloride 0.4 or 0.8 mg/ml or buprenorphine 0.03 mg/ml. The injected neuroleptic agent was droperidol 2.5 mg/ml, a solution without preservative and with a pH value similar to that of morphine chloride (3.5; pKa 7.64). Epidural droperidol was used in the following circumstances: increasing dose of epidural opioids had proven ineffective; a

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sudden increase in demand for epidural opioids, that is suspected development of tolerance; a sudden loss of effectiveness of epidural opioids. The position of the tip of the epidural catheter was tested either by radiography or by instillation of local anaesthetics.

The effectiveness of droperidol was assessed by looking at the total daily dose of epidural opioid, the number of daily injections of epidural opioids and by using a 0–4 pain relief scale (0, no relief, 1, slight relief, 2, moderate relief, 3, good relief and 4 complete relief). Any side effects were noted. The statistics used were nonparametric; Wilcoxon's test was used for paired differences and Mann Whitney U test for the comparison of two groups.

Results

During a period of one year (March 1983–March 1984) 119 patients suffering from chronic pain were subjected to long term treatment with epidural opioids (more than 7 days) injected via a catheter in the lumbar region. In 23 of these cases (19.3%), epidural droperidol was added. Three patients were not included in assessment of the results: one child, in whom scoring pain relief proved impossible, one adult with rapidly spreading malignant disease and one adult in whom the epidural opioids were discontinued.

The diagnoses of the 20 patients included are shown in Table 1. Seventeen patients (85%) suffered from malignant diseases and three patients (15%) from benign diseases (two fractured hips and one post laminectomy back pain). The median age was 64.5 years (range 32–87 years). Fifteen patients (75%) received morphine chloride and five (25%) buprenorphine. The median daily doses of epidural opioids are shown in Table 2.

Table 1. Main diagnoses of 20 patients treated with droperidol epidurally

3 Benign	
17 Malignant	
Lung and breast	3
Gastrointestinal	3
Urological	5
Gynaecological	3
Other	3

Prior to injection of droperidol, the daily dose of morphine chloride totalled 30 mg (range 12–32 mg) and of buprenorphine 1.35 mg (range 0.6–5.4 mg). Following epidural droperidol, the daily doses were reduced to 20 mg (range 4–40 mg) and 1.35 mg (range 0.6–1.35 mg) respectively. The values for morphine chloride were significantly different ($p < 0.05$). The number of daily dosages of morphine was also reduced significantly (Table 3), from 4 (range 2–5) to 3 (range 2–4) per day ($p < 0.05$) following epidural droperidol. No differences could be detected in the buprenorphine group, but when the groups are combined, the difference is significant. Pain relief scores increased significantly in both groups, as well as when combined (Table 4). The median values were 2 before and 4 after the administration of droperidol ($p < 0.01$). Altogether, 16 out of 20 patients showed an improved pain relief score (80%). The median daily dose of opioid was reduced with ten patients (50%) and the number of daily injections decreased with eight patients (40%).

The median daily dose of droperidol was 2.9 mg (range 1.25–30 mg) administered as 1.9 (range 1–6) injections. These figures are biased by the fact that one of the patients received an accidental daily dose of 30 mg of droperidol. In the case of one patient, a daily dose of 15 mg (3 × 5 mg) was completely ineffective. In all other cases, the usual dosage of droperidol amounted to 1.25–2.5 mg once or twice daily, given immediately prior to the instillation of epidural opioid.

Seven patients experienced unwanted side effects during treatment. Reversible Parkinsonism occurred with the patient who received the

Table. 2. Daily dose (mg) of opioid epidurally

	Number of patients	Median before droperidol	Median after droperidol	Median pair differences	Test for pair differences
Morphine	15 (75%)	30 (18–32)	20 (16–32)	8 (0–12)	$p < 0.05$
Buprenorphine	5 (25%)	1.35 (0.6–5.4)	1.35 (0.6–1.35)	0 (0–0)	NS

Brackets represent the first and third quartiles. NS: nonsignificant.

Table 3. Number of daily injections epidurally

	Number of patients	Median before droperidol	Median after droperidol	Median pair differences	Test for pair differences
Morphine	15	4	3	0	$p<0.05$
	(75%)	(3–5)	(2–4)	(1–2)	
Buprenorphine	5	3	3	0	NS
	(25%)	(2–6)	(2–6)	(0–0)	
Total	20	3	3	0	$p<0.05$
		(3–4)	(2–4)	(0–1)	

Brackets represent the first and third quartiles. NS: nonsignificant.

Table 4. Pain relief score (PRS)

	Number of patients	Median before droperidol	Median after droperidol	Median pair differences	Test for pair differences
Morphine	15	2	4	2	$p<0.01$
	(75%)	(1–2)	(3–4)	(1–2)	Significant
Buprenorphine	5	2	4	2	$p<0.01$
	(25%)	(1–2)	(2–4)	(0–2)	Significant
Total	20	2	4	2	$p<0.01$
		(1–2)	(3–4)	(1–2)	Significant

Brackets represent the first and third quartiles.

accidental dose of 30 mg of droperidol daily for several days. The disorder disappeared following treatment with biperiden. Six patients complained of sedation and these patients were receiving an average of 4.7 mg droperidol compared to 2.2 mg in those who did not have any sedation. A reduction in the dose to an average of 2.0 mg resulted in disappearance of this symptom. No other unwanted side effects were recorded. All patients were specifically asked about nausea and vomiting, bladder trouble, pruritus, dizziness, constipation and changes of the mood. There was no evidence of respiratory depression.

To investigate the toxic effect of epidural droperidol, the spinal medulla of a man who had been successfully treated with epidural droperidol in combination with epidural opioid for 4 months was examined at postmortem. No signs of necrosis, inflammation or other structural changes were found.

The pharmacokinetics of epidural droperidol were investigated in a small study comprising three patients. In one patient, we administered 5 mg of droperidol intravenously and in two patients 1.25 and 2.5 mg epidurally. The results showed some uptake of droperidol into the blood, whereas the drug could not be detected in the cerebrospinal fluid after intravenous administration. The blood concentrations after epidural administration were lower than after intravenous administration. We found no sedative or direct analgesic effect with the epidural doses.

Discussion

Potentiation of enterally/parenterally administered opioids by means of neuroleptic agents is a well known phenomenon. Tulunay and co-workers[5] showed that the use of dopamine receptor blocking agents lowered the ED_{50} of parenteral opioids. Other investigators have demonstrated independent and descending dopaminergic tracts in the spinal medulla.[2,3] Jensen and Smith[6] evaluated the effect of intrathecal dopamine agonists on the tailflick reflex in rats. Dopamine and apomorphine had an inhibitory effect on the response, which seems to be the opposite to our findings, but the effect could only be demonstrated in spinal animals and was not investigated in combination with opioids. The reaction may be different in awake, normal animals, but this has not been investigated. Kim and Stoelting[4] administered droperidol together with morphine intrathecally in normal rats. Addition of droperidol prolonged the duration of intrathecal morphine by 40%. Furthermore, droperidol seemed to inhibit development of tolerance.

A Danish multicentre study revealed that 33% of patients suffering from chronic pain and treated with epidural opioids required supplementary medication. This consisted of analgesics, neuroleptics (8%), and epidural local anaesthetics.[1] In rare cases, it has proven necessary to inject intrathecal phenol. Most of the mentioned combinations produce adverse effects, especially central nervous symptoms.

In treating cancer patients, we find it essential to reduce the incidence of unwanted side effects due to medication as much as possible and also to offer the simplest way of administering this treatment. In our study, three patients with nonmalignant diseases are included, but they were old and in a rather terminal state. In general, we try to avoid droperidol epidurally in patients with nonmalignant disease as the toxic effects are not fully evaluated.

Epidural droperidol seems to potentiate the effects of epidural opioids. In our study 80% of the patients had significantly better scores following its use. The median daily dose and median number of daily injections were reduced significantly in the morphine group, but not in the small buprenorphine group. It should be noted that in no patient was there a reduction in the degree of pain relief after administration of droperidol.

The only frequent side effect was sedation (six patients), a symptom that was eliminated following reduction in the dose of droperidol but without affecting pain relief. A comparison of the dose range indicates that the initial dose of droperidol must be low and adjusted on an individual basis, keeping in mind that major dosages may elicit catalepsy, as in the case of reversible Parkinsonism in our study.

In cancer patients, nausea and vomiting are regular complaints. We had hoped to see the anti-emetic effect of droperidol prove useful in our patients, but, surprisingly, there were no cases of nausea prior to droperidol administration.

The importance of central and placebo effects remains unknown in this retrospective study and an analgesic effect of droperidol remains to be clarified in a double-blind placebo study. Likewise, the target zone of droperidol (segmental ?) must be evaluated in pharmacokinetic studies. Our preliminary pharmacokinetic study revealed that the effect of droperidol cannot be explained solely by uptake into the blood, because of the relatively low concentrations. However, some central nervous effects must be expected.

In conclusion, we believe that droperidol, injected epidurally, may potentiate epidural opioids without increasing the incidence of unwanted side effects. Whenever the effect of epidural opioid is inadequate or tolerance develops, droperidol might be the supplementary drug of choice. The effective daily dosage of droperidol averages 2.5 mg/day distributed as two injections. It is advisable to start at approximately 1.25 mg/day due to individual variation and risk of sedation.

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Anaesthesia, 1986, Volume 41, pages 1120–1123

CASE REPORT

Narcotic-induced choledochoduodenal sphincter spasm reversed by naloxone

A case report and review

K. J. BIRD

Summary

A case report of biliary colic induced by narcotic premedication and reversed by naloxone administration is described and the literature reviewed.

Key words

Antagonists, narcotic; naloxone.
Analgesics, narcotic; papaveretum.

Narcotic analgesics are known to cause spasm of the choledochoduodenal sphincter (sphincter of Oddi). This may have two important consequences: upper abdominal pain in the awake patient, or failed passage of contrast medium during operative cholangiography, giving a false impression of distal common bile duct obstruction. Many drugs have been used with varying success to prevent or reverse this spasm. A patient is described who presented for non-biliary tract surgery and who, following premedication with papaveretum and hyoscine, experienced severe biliary colic which dramatically resolved on administration of naloxone.

Case history

A fit 27-year-old female with five children presented for laparoscopic sterilisation. Apart from cholecystectomy at the age of 19 years, her past medical history was uneventful. Fifteen minutes after premedication with papaveretum 15 mg and hyoscine 0.3 mg, she complained of severe colicky abdominal pain which she likened to that she experienced before her cholecystectomy. For 15 minutes the author observed a typical severe biliary colic whilst awaiting the arrival of naloxone. At the height of a colic 0.2 mg of naloxone was given intravenously and was followed by an almost immediate cessation of the pain. A further 0.2 mg was given intramuscularly and there was no recurrence.

The next day, after a premedication of pethidine 50 mg and promethazine 25 mg, she had an uneventful laparoscopic sterilisation. Follow-up investigations included normal liver function tests and a normal ultrasound of the biliary system. Surgical opinion was that the most likely explanation of the episode was a drug-induced biliary spasm.

Discussion

Both naturally occurring and synthetic narcotic analgesic drugs have been shown to increase intrabiliary pressure due to choledochoduodenal

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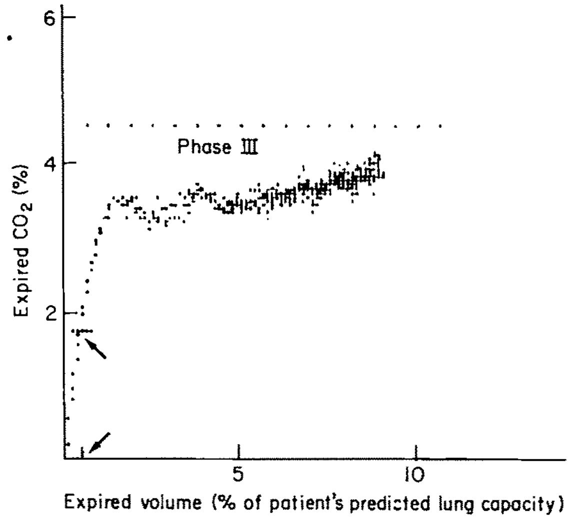

Fig. 3. A computer printout of one CO_2 single breath test. On the volume axis, the markings are 5 and 10% of the patient's predicted total lung capacity. The tidal volume is 470 ml. The dotted line above the tracing represents the CO_2% of a gas equilibrium with arterial blood. $V_{D_{aw}}$ is arrowed. Note the reduced airway deadspace and increased arterial–alveolar CO_2 difference, i.e. alveolar deadspace. The concave phase III is typical of severe airway obstruction.[3]

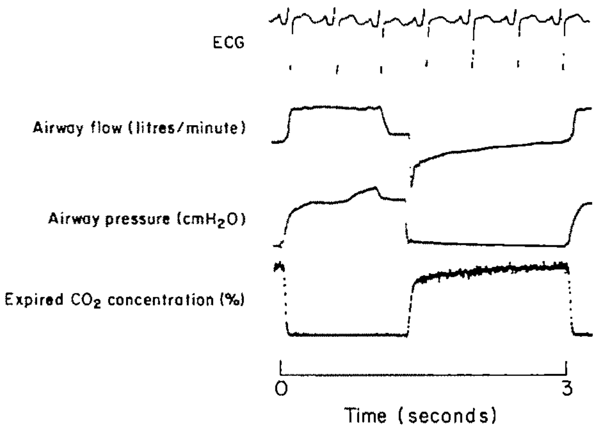

Fig. 4. After the thorax had been opened. Inspiratory time has been increased to 33% of cycle and the inspiratory flow is consequently less than previously. The inspiratory pressure curve is improved and there are no ECG-synchronous variations in flow or pressure. When the thorax was closed again, the appearance reverted to that of Fig.1.

adult. The shape of the tracing is unusual; phase III, the somewhat inappropriately termed 'alveolar plateau', is concave upwards, a sign of extreme obstruction.[3] In addition, it shows unusual irregularities, synchronous with the intermittent flow. Lastly, the airway deadspace $V_{D_{aw}}$ (which includes the tracheal tube) is extremely small (about 20 ml); normal intubated adult fifth and 95th percentiles are 58 and 127 ml.[5]

A small right anterior thoracotomy was performed. The tumour was seen to occupy much of the right hemithorax. There was some pleural fluid and the lung volume was obviously greatly reduced. After the chest was opened the inspiratory and expiratory flow became more normal, although the inspiratory pressure pattern was still abnormal (Fig. 4). When a biopsy of the tumour had been taken, the chest was closed, at which point the flow and pressure tracings reverted to their previous appearance.

The biopsy showed a non-Hodgkin lymphoma. After treatment for 4 days with steroids and cyclophosphamide, the chest Xray showed a great reduction in tumour mass. There was a considerable improvement in the expiratory flow tracing and a normal inspiratory flow. The boy was extubated without difficulty on the fifth day.

Discussion

The phenomena described here are due to compression of lung and airway. Because airway resistance is increased and the compliance of the compressed lung decreased, an unusually high pressure is generated during inspiration. The calibre of the narrowed airway is further modified by the heart's movement, hence the synchrony of the flow with the ECG. The inspiratory pressure curve is typical of mechanical obstruction, which reduces as inflation continues, i.e. as lung volume increases. Similar changes can be seen in severe asthma or when the opening of the tracheal tube is placed against the carina. End expiratory flow does not reach zero and this also indicates increased resistance.

The reduced V_{Daw} is also caused by the obstruction and small lung volume. It is likely that a 'pool' of CO_2-containing gas was retained in a major bronchus behind the obstruction and that this gas appeared at the airway opening soon after the tracheal tube (volume about 10 ml) had been flushed clear of the CO_2-free inspiratory gas. Thus, the obstruction must have been at the level of the main bronchus or carina, i.e. very close to the opening of the tracheal tube; this is in agreement with the Xray findings.

The sloping, upwardly concave phase III of the CO_2 single breath test (SBT-CO_2) is probably due to an increased spread of ventilation/perfusion ratios as the lung is ventilated at a reduced functional residual capacity (FRC), and to an increased tendency to airway closure and uneven gas distribution because of the bronchial occlusion. These changes are likely to be the cause of the increased alveolar deadspace fraction. Unusual SBT-CO_2 forms are sometimes seen during thoracotomy done for other reasons, such as when the surgeon retracts the upper lung. The fluctuations in expired CO_2 content represent variations in the flow of gas from different regions, which suggests that the airway obstruction was more pronounced on one side.

The extramural pressure on the airway was relieved when the chest was opened and thus reduced the degree of obstruction. This increased again when the chest was closed. Presumably, in the awake state, the obstruction was less pronounced because of the greater FRC.

We have recently observed another case of intrathoracic non-Hodgkin lymphoma in a 9-year-old girl. Her tumour was proportionately smaller and there was no intermittent obstruction to flow during controlled ventilation. Nevertheless, the SBT-CO_2 curve was concave on most breaths, the alveolar deadspace fraction was increased at 0.19 and the arterial to end-tidal P_{CO_2} gradient was 0.5 kPa. She too required postoperative ventilation, but was extubated after 24 hours of treatment. It should be noted that even a single pre-operative dose of steroids can make the histological diagnosis of non-Hodgkin lymphoma impossible; it was therefore necessary to anaesthetise both patients without any pre-operative therapy aimed at reducing tumour size.

Acknowledgment

The authors thank Professor Björn Jonson for the loan of the computer.

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Anaesthesia, 1986, Volume 41, pages 1139–1142

APPARATUS

Respiratory monitoring with a new impedance plethysmograph

S. HOFFMAN, R. JEDEIKIN AND D. ATLAS

Summary

A new impedance plethymograph respiratory monitor, (AR-8800), was tested on anaesthetised dogs. Decreases in tidal volume and total apnoea were brought about by partial and complete airway obstruction and by partial and total muscle paralysis. The changes in respiration were reliably detected by the monitor and its alarms activated within 15–20 seconds. The misinterpretation of gross body movement as normal breathing did not occur. Our findings suggest that the AR-8800 is a safe and dependable monitor which has distinct advantages and may be of particular use in the monitoring of patients at risk of developing respiratory depression or obstruction, whether in the intensive care unit, the general ward or at home.

Key words

Monitoring; ventilation.
Measurement techniques; impedance plethysmography.

Noninvasive monitoring of breathing in both acute and chronic clinical situations has received relatively little attention and technological breakthroughs in this field have been limited. The need for dependable monitors has, however, been fully appreciated and in recent years there have been some advances in the manufacture and use of apnoea monitors and alarms.[1]

The indications for respiratory monitoring include patients at risk following surgery and anaesthesia, patients receiving epidural or spinal opioid analgesia, respiratory cripples requiring sedation and analgesia, patients suffering from head injuries or drug overdose and children with increased susceptibility to attacks of apnoea and the sudden infant death syndrome.

Most modern apnoea monitors employ electrical impedance to detect the respiratory waveform and to provide an alarm should there be a cessation of breathing for a preset time period. A major problem encountered in most current impedance monitors is their inability to alarm for partial respiratory depression or for either complete or partial upper airway obstruction accompanied by ineffectual chest movement. These ineffectual chest movements and attempts at gasping for air are frequently interpreted by impedance monitors as normal respiratory wave forms, thereby inhibiting the early activation of the alarm. Similarly, the mechanical action of the heart modulating the transthoracic impedance may be detected and interpreted by the monitor as breathing during a period of apnoea.

In order to overcome these problems, the AR-

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8800 respiratory monitor was developed and its efficacy tested on five anaesthetised dogs.

Methods

Five mongrel dogs, mean weight 15 kg, were used in the evaluation of the monitor. The dogs were anaesthetised with intravenous pentobarbitone 30 mg/kg: their tracheas were intubated and they were allowed to breathe air spontaneously. Intravenous and intra-arterial catheters were inserted and the arterial cannula was attached to a strain gauge transducer for systemic blood pressure monitoring and blood gas sampling. Tidal and minute volumes were measured with an East Spirox electronic spirometer attached to the exterior end of the tracheal tube.

The respiratory monitor, AR-8800, was attached to the dog by two pairs of standard pre-gelled ECG monitoring electrodes. Two electrodes were placed on each side of the chest at the site of maximum rib cage expansion; the sites were first shaved and cleaned with ether to ensure good electrical contact.

One hour after the induction of anaesthesia, the following procedures were performed and recorded on a two-channel pen recorder at a speed of 5 cm/minute: total obstruction of the tracheal tube by clamping for periods of 15–45 seconds. The dog was allowed to return to a steady state, which was confirmed by return to normal of the pulse rate (90–110 beats/minute), tidal volume (180–220 ml) and respiratory rate (13–17 breaths/minute) before the next evaluation. The time taken to return to the steady state was 15–30 minutes. Partial obstruction of the tracheal tube by 50% was achieved with a screw clamp; this maintained the tidal volume at approximately half of the baseline volume for periods of 15–45 seconds; adequate time was allowed for a return to the steady state between tests. Partial respiratory muscle paralysis was induced with 0.05 mg suxamethonium. Full respiratory muscle paralysis was induced with 1 mg of intravenous suxamethonium. Simulation of gross chest movement was accomplished by pushing and pounding the chest wall.

The function of the auditory and visual alarms was noted and recordings made of the absolute rectified respiratory waveform as well as the respiratory volume index curve. The absolute rectified respiratory waveform is proportional to the actual incremental impedance waveform, which is a function of the mechanical a breathing. The respiratory volume index the computed ratio of the subject's ventilation and his initial ventilation l each is a 15-second integral average respiration waveforms (hereafter, volume). Both these curves may be selec viewed on the analog meter of the AR-

The following AR-8800 alarms were a and observed: volume index (VI) alar alarm was activated by a fall in VI to preset value (0–100% of baseline) or by an in VI to above a preset value (100–150% line); the apnoea alarm was activated wh was absence of breathing during a selec period (7.5–20 seconds). The motion motion light (no audible alarm) was acti gross body movement artefacts. A pr period of gross movements inhibits integration, leading to a VI alarm; he alarm (high and low preset limits); alarms, activated for loose leads, impro sitivity settings and low battery voltag tests were repeated on five different dog

Results

Complete obstruction of the trache resulted in the activation of the volume in and heart rate alarms within 15 seconds. the period of obstruction there was cessation of ventilatory exchange and a re of tidal and minute volumes recorded spirometer to zero. An artefactual wavef recorded due to chest wall movement as attempted to overcome the obstruction pseudo-respiratory movements did not, h inhibit activation of the VI alarm. The resumed ventilation with immediate cess the VI alarm on removal of the obst However, post obstruction hyperven activity now followed, which was detecte 15 seconds by the high setting of the V (Fig. 1).

During partial obstruction of the trache the tidal volume was reduced by half to This decrease in volume was sensed monitor and the VI alarm was activated w minute volume had dropped to 50% baseline. At this point a reduction amplitude of the respiratory wavefor recorded. (Fig. 2). With the release of the hyperventilation occurred, which was

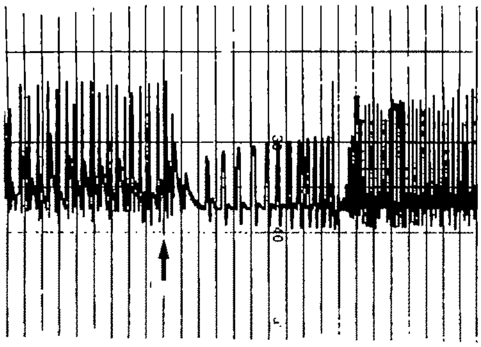

Fig. 1. Changes in the absolute rectified respiratory waveform following complete obstruction of the tracheal tube. Despite complete obstruction, smaller and less frequent, but normal-looking waveforms are recorded. On removal of the clamp an increase in amplitude and in frequency of the respiratory waves is seen.

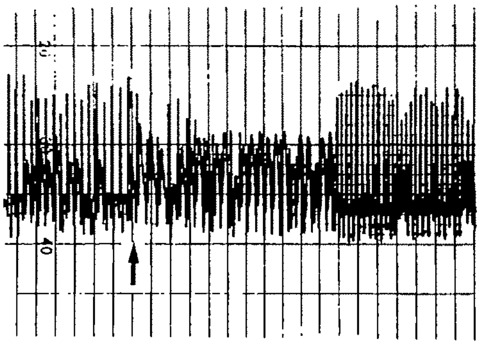

Fig. 2. Reduction in amplitude of respiratory waveforms following partial obstruction of the tracheal tube.

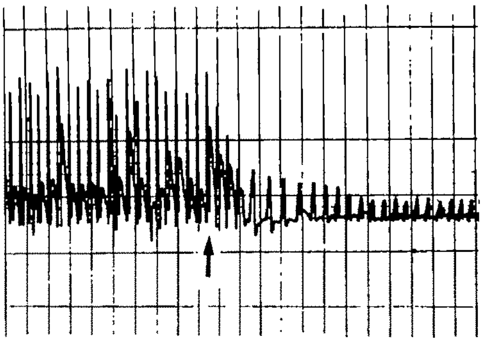

Fig. 3. Decreased amplitude of absolute rectified respiratory waveform after suxamethonium associated with a measured decrease of tidal volume to 50 ml.

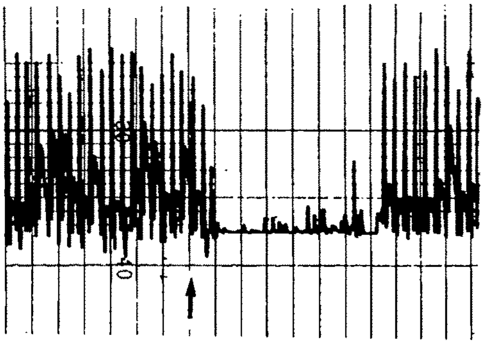

Fig. 4. Decreased amplitude of abnormal respiratory waveform caused by rapid pounding on the dog's chest.

after 15 seconds by the high limit setting of the VI alarm. During both partial and total airway obstruction, only the VI alarm responded to the respiratory changes, whereas the apnoea alarm was not activated.

Partial muscle paralysis with suxamethonium caused the tidal volume to fall to 50 ml, setting off the VI alarm (Fig. 3). The apnoea alarm remained insensitive to the marked reduction in tidal volume and only with total respiratory muscle paralysis did activation of the apnoea alarm occur.

Simulation of gross chest movement by pushing and pounding the dog's chest resulted in the disappearance of the usual respiratory waveform and the triggering of the VI alarm (Fig. 4). However, simultaneous activation of the motion light by these movements indicated that these movements were artefacts.

Discussion

Normal breathing causes amplitude and/or frequency modulation of the oscillation signal. It may thus provide a read-out of respiratory frequency as well as indicating apnoea. A major disadvantage of the usual impedance plethysmograph respiratory monitor is that it only responds to a state of apnoea and has not the facility to recognise gradual or sudden decreases in tidal or minute volume. This seriously limits patient care, in that early recognition of deteriorating respiratory function is delayed until apnoea occurs, which may at this stage be irreversible.

The distinct advantage of the AR-8800 over other impedance plethysmograph respiratory monitors of which we are aware is its ability to detect and respond to volume changes in respiration. This facility has been confirmed by our present study, in which we were able to detect varying degrees of reduction in minute volume as a result of partial airway obstruction, as well as in partial respiratory muscle paralysis. These deviations from the previously measured baseline of the dogs' normal ventilation were detected within 15 seconds of their onset. With the AR-8800, spontaneous ventilation at rest is reflected as an integrated baseline of 100% which is computed and stored by the monitor. Thus, any changes in breathing and in chest movement on respiration are reflected as changes above or below the 100% baseline. The VI alarm that detects these changes can be set to signal at any percentage change desired, as well as having a time delay.

A serious problem that arises when monitoring respiratory failure with an impedance plethysmograph respiratory monitor has been the inability to detect airway obstruction. Upper airway obstruction is usually accompanied by varying degrees of respiratory muscle activity in the subjects' efforts to overcome the obstruction. With usual impedance plethysmographs, these ineffectual respiratory movements are sensed by the monitor and wrongly interpreted as being normal effective ventilatory movements. In this state of complete airway obstruction a warning alarm is thus not sounded until all breathing movements have ceased and total apnoea has occurred. As seen in our experiments, this defect was overcome by the AR-8800 which is able to differentiate between effective and noneffective respiratory movements. The independently acting apnoea alarm became activated only when total apnoea occurred and when all respiratory and other movements had ceased.

The VI alarm proved so consistently reliable in all situations that the inclusion of an apnoea alarm appears redundant, although it does serve a good purpose as a support alarm. Cardiac and respiratory rate digital monitors are useful additional features on the monitor.

Conclusion

The AR-8800 appears to be a marked improvement on present impedance plethysmograph respiratory monitors. It fulfills the need of a non-invasive monitor of respiration which responds to early changes and is not dependent on apnoea alone for its activation.

The AR-8800 apnoea cardiorespiratory monitor is manufactured by Atlas Researches. Hod Hasharon, Israel.

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Anaesthesia, 1986, Volume 41, pages 1143–1145

Forum

Sleep and comfort after Caesarean section

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Summary

To compare postoperative well-being after general and epidural anaesthesia, 58 women undergoing Caesarean section were divided into a general anaesthetic group receiving intramuscular opioid postoperatively (26), and an epidural group receiving morphine via the epidural route (32). The epidural group required less analgesia ($p < 0.01$ at 0.5 and 8 hours, $p < 0.001$ at 4 hours). There was no difference in the use of oral analgesics. At 1, 4 and 24 hours after delivery more patients in the general anaesthesia group described themselves as very comfortable ($p < 0.05$). More in the epidural group had a very good night's sleep during each night studied. Patients in the epidural group were slower to use the ward toilet ($p < 0.01$) and had more itching ($p < 0.001$). Our conclusion is that patients progressed well in both groups.

Key words

Anaesthesia; obstetric.
Pain; postoperative.

Maternal mortality associated with general anaesthesia for Caesarean section, disappointingly, has been constant in recent years,[1] and has prompted interest in epidural anaesthesia as perhaps a safer alternative. An impression that postoperative well-being is improved following epidural anaesthesia has some support,[2] but requires further appraisal.

This study examines aspects of postoperative comfort following epidural anaesthesia and compares it with that following a general anaesthetic in patients undergoing Caesarean section. In addition, an assessment was made of speed of recovery and analgesic requirements of the two groups.

Method

We examined 58 healthy women undergoing delivery of a single fetus by elective lower segment Caesarean section (Table 1). Patients were allocated into a general anaesthetic group ($n = 26$), or an epidural group ($n = 32$) as appropriate after consideration of the wishes of the patient and the indication for the operation.

Our usual anaesthetic practices were adhered to in both groups. Peri-operative analgesia was provided either with intravenous followed by intramuscular papaveretum 10–20 mg in those given general anaesthesia, or local anaesthetic followed by 2–4 mg of preservative free morphine in 10–20 ml of normal saline via the epidural catheter in the epidural group. Any patient who, having received epidural morphine, was considered to need further opioid administration within the first 12 hours following delivery, was referred for management to the on-call anaesthetist. Postoperatively, analgesia was supplied initially by intramuscular opioids, then oral opioids (dextropropoxyphene–paracetamol or buprenorphine) and then aspirin or paracetamol.

Patients were given a proforma on which to record their postoperative progress as follows: analgesia administered, the occurrence of nausea and itching and incidence of difficulty with micturition. The initial responses were made under the supervision of an anaesthetist and, in addition, patients were seen daily by an anaesthetist.

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Table 1. Patient data

	General anaesthesia	Epidural
n	26	32
Age (years)		
mean	26	29
range	18–39	21–44
Primips	7	10

Speed of recovery was assessed by noting the time taken to achieve certain milestones: the ability to sit up in bed and then to get out of bed, to walk around the room and then around the ward and to use the ward toilet. Patients were also required to complete at 10-cm linear analogue pain (very comfortable to worst pain imaginable) and sleep (good night's sleep to worst night ever) score at intervals up to 72 hours after delivery. These were subsequently divided into quarters and the number of responses in each quarter noted.

Statistical comparisons were made using the Chi square test with Yates' correction or Mann-Whitney as appropriate.

Results

Figure 1 shows the sleep scores (good, 0–2.5 cm, 2.5–5 cm, 5–7.5 cm, 7.5–10 cm, bad) for each of the three nights following delivery. Although there was no overall significant difference between groups, more epidural patients had a very good night's sleep during each night studied.

Figure 2 shows analgesic requirements in the two groups. Up to 4 hours, 97% of the epidural group had received no extra analgesia and at 8 hours it was still 84% ($p < 0.01$ at 0.5 and 8 hours and $p < 0.001$ at 4 hours). This difference is reflected in the number of patients receiving general anaesthesia who received an intramuscular opioid ($p < 0.01$ at 0.5, 4, 8 and 12 hours). There was no significant difference in the use of oral analgesics such as dextropropoxyphene–paracetamol combination or paracetamol alone. However, at 1, 4 and 24 hours after delivery, statistically more of the general anaesthetic group described themselves as being very comfortable ($p < 0.05$).

Table 2. Recovery times (hours, SD) of patients following Caesarean section with either an epidural or a general anaesthetic

Milestones	General anaesthesia	Epidural
Sitting up	5.67 (6.30)	2.82 (3.72)
Getting up	17.36 (4.42)	16.98 (3.79)
Ward toilet	19.00 (8.77)	27.77 (8.46)**
Walking	20.65 (8.87)	21.55 (7.29)
Out and about	31.48 (11.64)	36.28 (10.00)

**, $p < 0.01$.

Table 2 illustrates the variability seen in both groups in the time taken to reach their milestones. It should, however, be noted that both groups were up and walking about within 20 to 36 hours following delivery. There was a statistically significant difference between the two groups ($p < 0.01$) in the time taken to use the ward toilet; the general anaesthesia group were the first to pass urine unaided (11 hours, range 1–48 hours), while the epidural group took 25 hours (range 24–48 hours). Some patients used a bedpan before visiting the ward toilet.

Of the patients given general anaesthesia, 11% noticed itching compared with 75% of the epidural group ($p < 0.001$). None, however, complained of it spontaneously and no patient found it troublesome. Nausea

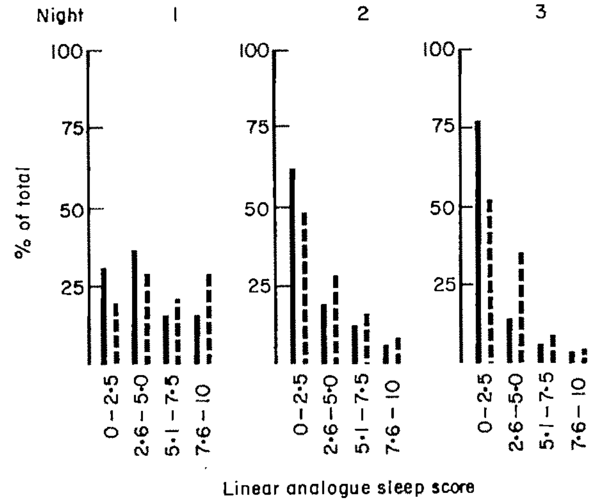

Fig. 1. Linear analogue sleep scores, divided into four parts, for both groups of patients on each of the first three post-operative nights. (0 best–10 worst). ——, Epidural group; ——, general anaesthesia group.

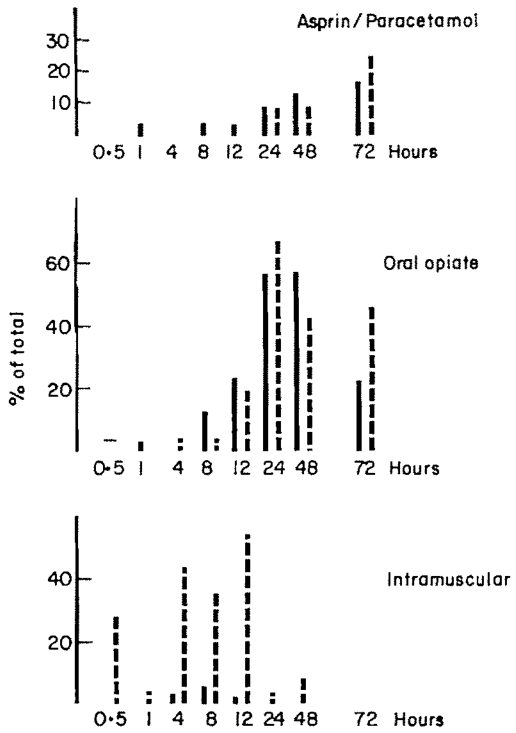

Fig. 2. Requirements for analgesics in both groups over the first three postoperative days. ——, Epidural group; ----, general anaesthesia group.

was more common in the epidural group (31% compared to 19%), but the difference was not significant. However, prochlorperazine was given frequently to those who had general anaesthesia along with their requirement for intramuscular opioid.

Discussion

General anaesthesia for Caesarean section has a number of accepted complications. An audit of 370 general obstetric anaesthetics carried out during the course of this study showed that 42% of patients experienced sore throats attributed to tracheal intubation, 17% experienced muscle pains attributed to suxamethonium use, 6% dreamt during the operation and 1–2% recalled a voice or an event that could be directly related to the operation. All patients were visited post delivery by a physiotherapist, but 3% were considered to need extra physiotherapy with or without a course of antibiotics, because of a productive cough. Most if not all of these problems could be avoided by using epidural anaesthesia. Despite this, both groups in the study made what we consider to be a rapid recovery, although patients in the epidural group appeared to be retarded by the presence of a self-retaining urethral catheter. Review of patient data showed that patients had their catheters removed the following morning, regardless of the time of delivery. This would suggest that time spent catheterised might be more the product of rigid ward routine than patient need.

The reduced analgesic requirements of patients in the epidural group who received a single small dose of morphine epidurally is demonstrated for up to 12 hours after delivery, although multiple intramuscular injections of opioid given to the general anaesthetic group produced equivalent analgesia. No attempt was made to regulate the timing of drug administration with completion of linear analogue scores. It is probable, therefore, that patients who had a general anaesthetic would have been scoring sleep and comfort against a background of fluctuating blood levels of analgesic, more so than the patients in the epidural group. Consequently, the responses of those given general anaesthesia would have been dictated by the relationship of the time of scoring to the previous injection. This would explain why more responses in this group were towards the extremes of the linear analogue. It would also explain why a beneficial effect was observed on sleep in the epidural group, although this was not statistically significant.

Despite minor complications related to general anaesthesia, patients progressed well in both groups and these results fail to confirm our impression that patients who receive epidural anaesthesia followed by epidural morphine have a superior postoperative course than those who receive general anaesthesia and intramuscular opioid analgesia.

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Can epidural catheters penetrate dura mater? An anatomical study

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Summary

A study using postmortem dura mater and arachnoid mater showed that catheter perforation of dura did not occur. In contrast, perforation of arachnoid proved easy.

Key words

Equipment; catheters, epidural.

Perforation of spinal dura mater by epidural catheters is a described complication of epidural anaesthesia;[1] the resulting subarachnoid blockade occurs early or late in the course of continuous catheter techniques. A study was performed using postmortem material to assess the extent of this problem.

Methods

Sections of postmortem dura and arachnoid mater were obtained from three levels from 10 adult spines (cervical, thoracic and lumbar). All specimens included posterior midline dura. The dura was peeled off the arachnoid and the outer surface wiped dry before each experiment. The specimens were pinned to a workbench by one end and held taut. The arachnoid mater was tested *in situ*, remaining moist but with no supporting cerebrospinal fluid (Fig. 1).

Three epidural catheters were tested on each specimen. These were the Vygon 19-G open end and Portex 16- and 18-G three helical eye catheters. A previous study showed that the Vygon 19-G and Portex 16-G exerted a similar degree of force despite having different tip shape.[2] The catheters were supported to within 5 mm of their tips, using an epidural needle with the tip removed. Each catheter was held, in turn, and attempts were made to perforate dura or arachnoid using as much force (unmeasured) as possible with the catheter tip held perpendicular to the tissue.

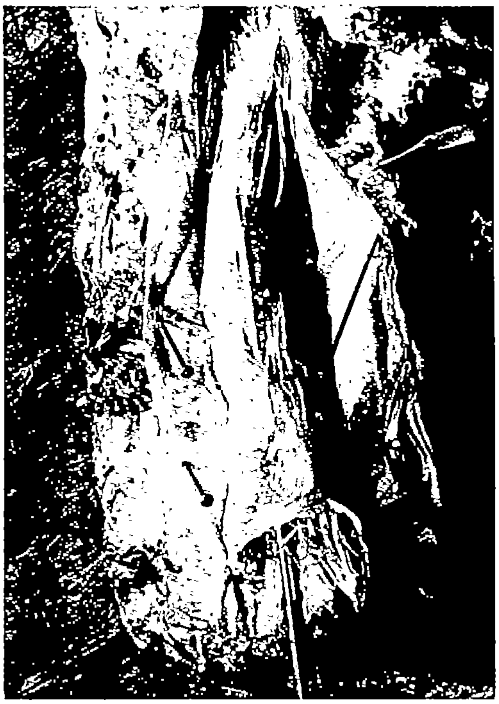

Fig. 1. Lumbar spine with dura mater divided to expose the arachnoid membrane for testing, supported by a centimetre marked needle.

Table 1. Spinal level and membrane perforated

Region	Dura	Arachnoid
Cervical	−	+
Thoracic	−	+
Lumbar	−	+

+, Perforation; −, no perforation.

Results

At no time did any of the catheters tested penetrate any of the specimens of dura mater (Table 1). The dura was observed to be fairly compliant and stretched by up to

10% during each test. Arachnoid mater, on the other hand, was penetrated easily in all cases. Initial resistance to penetration was elicited by the thinner Portex catheters. Less than maximal force was required in all cases.

Discussion

Subarachnoid placement of catheters has a reported incidence of 0.57% in general surgical patients[3] and of 0.2% in obstetric cases.[4] Spinal dura is a substantial structure varying in thickness from 2.5 mm at cervical levels to 0.5 mm in the lumbar region.[5] It is composed of both fibrous and elastic tissue and is moderately compliant, demonstrating a range of movement during myelography under a range of applied pressures and body movements.[6]

In a review of individual reported cases there is no direct evidence to support the statement that catheter penetration of dura mater *per se* had occurred. In one case the epidural dose of local anaesthetic was injected through the needle before inserting a catheter.[7] Subsequent top-up through the catheter was found to be subarachnoid. It is quite probable that the initial injection through the needle was subdural and not epidural and that subsequent perforation of the arachnoid took place. In another such case, widespread blockade occurred and cerebrospinal fluid could be aspirated through the catheter.[8] Again, from the description it is quite probable that initial subdural placement had occurred. Subdural placement of epidural catheters is well recognised.[9]

It is estimated that the subdural placement of needles occurs in up to 5% of attempts at myelography[1] and an incidence of 7% has been reported in chronic pain patients.[10] The incidence in surgical or obstetric practice has not been defined. In one reported series of 352 continuous epidurals a low pressure headache was present in 38 cases (10.8%); four of these patients required epidural blood patch.[11] In no case had overt dural puncture or subarachnoid blockade occurred, although dural extra-arachnoid puncture by the needle may have taken place.

In the present study, an artificial arrangement was used in order to minimise slippage and to enable the maximum force to be exerted. Under these conditions it was found that intact dura mater could not be penetrated by the epidural catheters tested. In contrast, arachnoid mater provided little resistance to catheter perforation.

It is proposed that subarachnoid placement of epidural catheters occurs as a result of initial subdural needle placement. Transarachnoid migration of a catheter from the subdural to the subarachnoid space may complicate the course of a continuous catheter technique.

Acknowledgments

The author would like to express thanks to Dr J. Wilson and Dr D.B. Scott, Consultant Anaesthetists at the Royal Infirmary of Edinburgh, for helpful advice and discussion; also to Dr J.M.D. Hider, Lecturer in Anatomy at the University of Edinburgh, for access to specimens.

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Alfentanil in an anaesthetic technique for penetrating eye injuries

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Summary

Alfentanil in three doses (10, 20 and 30 μg/kg) was added to an anaesthetic technique suitable for penetrating eye injuries. All three doses proved effective in abolishing the marked present response to tracheal intubation which occurs with this technique, but at least 20 μg/kg was needed to obtund the heart rate response significantly and to facilitate early intubation. Transient hypotension and bradycardia occurred in some patients who received the highest dose of alfentanil. The incidence of postoperative sequelae was small in all groups. Thus, the optimal dose of alfentanil in an anaesthetic technique for penetrating eye injuries appears to be 20 μg/kg.

Key words

Analgesics; alfentanil.
Surgery; ophthalmic.

The rapid onset and short duration of action of alfentanil are attractive features for ophthalmic anaesthesia. In penetrating eye injuries, attention has recently been drawn to the detrimental haemodynamic and intra-ocular pressure changes which may occur when the currently recommended anaesthetic technique is used.[1–3] Alfentanil has been shown to abolish or reduce the rises in blood pressure and heart rate which occur after laryngoscopy and intubation.[4] We therefore investigated the haemodynamic changes during an anaesthetic technique recommended for penetrating eye injuries and studied the ability of three different doses of alfentanil to attenuate these changes. In addition, the intubating conditions, the incidence of postoperative vomiting and pain and the analgesic requirements were noted.

Methods

Informed consent was obtained from 48 patients, ASA class 1–3, scheduled for extracapsular cataract extraction and intra-ocular lens implantation under general anaesthesia. Patients with dysrhythmias and those where difficulty was expected with tracheal intubation were excluded from the study. The patients were randomly allocated to one of four groups: group 1, no alfentanil; group 2, alfentanil 10 μg/kg; group 3, alfentanil 20 μg/kg; group 4, alfentanil 30 μg/kg. Premedication was with oral temazepam, 10 or 20 mg, given 2 hours pre-operatively.

On arrival in the anaesthetic induction room, monitoring of blood pressure and heart rate was commenced with a Dinamap 1846 automatic blood pressure recorder and an electrocardiograph. A record of heart rate, systolic, mean and diastolic blood pressures was made every one minute. An 18 gauge intravenous cannula was sited in the dorsum of the left hand. Patients were pre-oxygenated for 3 minutes and baseline blood pressure and heart rate readings were obtained. Vecuronium, 0.15 mg/kg (i.e. 3 × ED_{95}) was injected, followed immediately by the chosen dose of alfentanil or water for injection. After 30 seconds, thiopentone 5 mg/kg was injected and cricoid pressure applied. Sixty seconds after the vecuronium had been given, the trachea was intubated. Intubating conditions were graded and scored (Table 1). Ventilation with 67% nitrous oxide and 33% oxygen was commenced and further blood pressure and heart rate measurements were noted over the next 3 minutes and subsequently in the operating theatre.

Table 1. Scoring of intubating conditions

Assessment	criteria	Score
Good:	cords relaxed, immobile and abducted	0
Adequate:	cords relaxed, immobile but not abducted	2
Poor:	cords mobile	4
	coughing or straining after intubation	4
	movement of limbs after intubation	2

Results

There were no significant differences between groups in terms of age, sex, weight, pre-induction blood pressures or heart rates (Table 2).

Table 2. Patient data. Mean (SEM)

Alfentanil dose (μg/kg)	n	M:F	Age (years)	Weight (kg)	Pre-induction BP mmHg Systolic	Mean	Diastolic	Pre-induction heart rate (beats/minute)
0	12	1:2	68.6 (4.07)	66.4 (5.56)	149.7 (5.87)	102.8 (3.71)	81.7 (4.21)	73.6 (2.79)
10	12	1:2	74.1 (2.60)	59.3 (3.13)	137.9 (5.15)	99.9 (3.65)	78.8 (3.84)	76.7 (4.49)
20	12	1:2	76.4 (2.40)	62.0 (3.86)	167.0 (10.67)	118.7 (6.81)	91.4 (5.23)	69.8 (3.24)
30	12	1:2	72.8 (2.64)	62.1 (2.55)	162.6 (7.28)	115.8 (7.00)	90.8 (5.22)	79.7 (4.65)

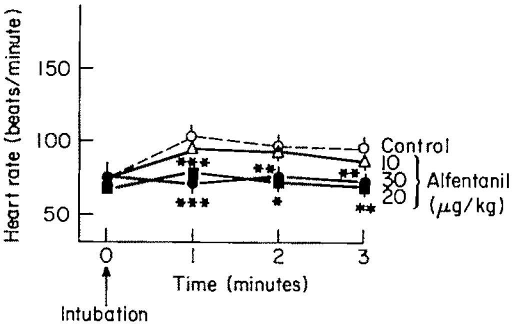

Fig. 1. Changes in mean blood pressure after intubation. Mean (SEM). ○, Control; △, alfentanil 10 μg/kg; ■, alfentanil 20 μg/kg; ●, alfentanil 30 μg/kg. *p > 0.05; **p > 0.01; ***p > 0.001.

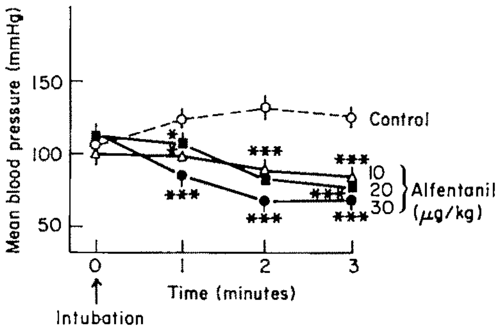

Fig. 2. Changes in heart rate after intubation. Mean (SEM). ○, Control; △, alfentanil 10 μg/kg; ■, alfentanil 20 μg/kg; ●, alfentanil 30 μg/kg. *p > 0.05; **p > 0.01; ***p > 0.001.

Intubating conditions one minute after vecuronium were significantly improved by the higher doses of alfentanil (Table 3). Five patients in the control group and three patients who received alfentanil 10 μg/kg coughed or strained after intubation. No patients who received alfentanil 20 or 30 μg/kg coughed or strained and all had good or adequate intubating conditions.

The increases in systolic, mean and diastolic blood pressures after intubation were significantly attenuated by all doses of alfentanil, but at least 20 μg/kg was required to attenuate the rise in heart rate (Table 4, Figs 1 and 2). With the higher doses of alfentanil, transient hypotension occurred. In three cases, this was associated with bradycardia (less than 50 beats/minute). Administration of atropine 0.2 mg to these patients corrected both the slow heart rate and low blood pressure. One patient required naloxone to antagonise the respiratory depressant effect of alfentanil 30 μg/kg.

Pain in the first 12 hours postoperatively, as assessed by verbal pain scores, was significantly reduced by all three doses of alfentanil (Table 5). Those who received alfentanil 20 or 30 μg/kg continued to have low pain scores for a further 12 hours. The incidence of vomiting and the need for postoperative analgesia was not significantly altered by the addition of alfentanil to the technique and indeed was low in all groups.

Discussion

The currently recommended technique for patients with penetrating eye injuries comprises pre-oxygenation, establishment of reliable intravenous access, administration of one and half times the normal intubating dose of a non-depolarising muscle relaxant ($ED_{95} \times 3$) followed, after a short delay, by thiopentone, cricoid pressure, laryngoscopy, intubation and moderate hyperventilation with nitrous oxide, oxygen and a volatile agent.[3] This technique may have to be adapted if a difficult intubation is anticipated, in the presence of other injuries (e.g. to the cervical spine) or in the presence of a full stomach. Indeed, the preservation of the injured eye may have to take its place in an order of priorities depending on the overall clinical presentation. In the uncomplicated case, it is rarely detrimental to allow a period of fasting and, during this time, metoclopramide and antacid prophylaxis may be given.

Developments of the technique aimed at allowing earlier tracheal intubation have become possible in the light of recent studies. Priming with a small dose of non-depolarising relaxant prior to the main dose may speed the onset of relaxation.[5] Atracurium provides earlier satisfactory intubating conditions than vecuronium or pancuronium.[6] However, its greater propensity

Table 3. Intubation scores 1 minute after vecuronium 0.15 mg/kg with and without alfentanil

	Alfentanil (μg/kg)			
	0 (Control)	10	20	30
n	12	12	12	12
Intubation score	3.7	3.3	1.0	0.2
Mean (SEM)	(0.77)	(1.05)	(0.52)	(0.17)
Significance of difference from control group			$p < 0.05$	$p < 0.01$

Table 4. Maximum change from pre-intubation readings of blood pressure (systolic, mean, diastolic) and heart rate in the first three minutes after intubation. Mean (SEM)

	Alfentanil dose (μg/kg)			
	0 (Control)	10	20	30
n	12	12	12	12
Δ Systolic BP (mmHg)	+27.2 (8.01)	−25.3† (11.73)	−49.2‡ (11.28)	−69.6‡ (5.32)
Δ Mean BP (mmHg)	+30.2 (6.74)	−14.2† (9.74)	−33.4‡ (9.46)	−47.4‡ (4.07)
Δ Diastolic BP (mmHg)	+24.5 (7.75)	−6.4† (7.58)	−30.7‡ (6.17)	−32.2‡ (3.54)
Δ Heart rate (BPM)	+29.8 (7.64)	+20.4 (4.74)	+6.3* (6.71)	−2.2† (6.05)

*, for $p < 0.05$.
†, for $p < 0.01$.
‡, for $p < 0.001$.

Table 5. Postoperative assessment of pain, nausea, vomiting and requirement for postoperative analgesia

	Alfentanil dose (μg/k)			
	0 Control	10	20	30
n	12	12	12	12
Verbal pain score for first 12 hours (mean)	2.4	1.1*	0.6†	0.08‡
Verbal pain score for second 12 hours (mean)	1.1	0.3	0.16*	0.16*
Incidence of nausea and vomiting	0	1	0	1
Number requiring post-operative analgesia	3	1	0	0

*$p < 0.05$.
†$p < 0.01$.
‡$p < 0.001$.

for causing dose-dependent histamine release is a disadvantage.[7,8] Monitoring of the offset of atracurium neuromuscular blockade must also be much more attentively looked for as patient movement during intra-ocular surgery may be disastrous.[9]

Despite the use of the new non-depolarising relaxants, the injured eye remains at risk from the ocular hypertensive effect of laryngoscopy and tracheal intubation.[2] This is especially true in penetrating eye injuries, where the initial intra-ocular pressure is close to atmospheric pressure and where autoregulation of choroidal blood flow may be lost.[10] Large rises in systemic arterial pressure, which may occur after laryngoscopy and tracheal intubation,[11] or rises in venous pressure after coughing or straining, may cause extrusion of ocular contents.[2] We found a marked pressor response to laryngoscopy and intubation in our control group using a technique suitable for penetrating eye injuries (Fig. 1) and this does not seem to have been previously documented. It has only very recently been recognised that marked rises in intra-ocular pressure can occur despite unchanged systemic arterial pressure when the 'penetrating eye' anaesthetic technique is used[1] and we are at present studying this aspect of our technique.

This study focussed on the haemodynamic effects of laryngoscopy and tracheal intubation and the intubating conditions at one minute. Several methods have been advocated to attenuate or abolish the pressor response to laryngoscopy and tracheal intubation. These include increasing the depth of anaesthesia by giving an increment of induction agent, lignocaine mouthwash and gargle, lignocaine 2 mg/kg applied topically by spray to the larynx and trachea, intravenous lignocaine 1.5 mg/kg, intravenous practolol, 0.4 mg/kg, intravenous sodium nitroprusside 0.1 μg/kg, intravenous droperidol 0.15 mg/kg and intravenous fentanyl 5 μg/kg.[12] More recently, alfentanil 15 or 30 μg/kg was noted to be as effective as fentanyl 5 μg/kg in abolishing the pressor response to laryngoscopy and tracheal intubation.[4]

We found that, using a technique suitable for penetrating eye injuries, the pressor response to laryngoscopy and intubation was abolished by alfentanil in doses from 10 μg/kg upwards while 20 μg/kg was needed to attenuate the heart rate response significantly. We also found that alfentanil 20 μg/kg and 30 μg/kg significantly improved intubating conditions at one minute.

The heart rate-dependent hypotension seen in three out of twelve patients who received alfentanil 30 μg/kg is a predictable problem of the combination of alfentanil and vecuronium and suggests particular vigilance at the time the eye is manipulated in case an oculocardiac reflex should be induced.

Alfentanil in a dose of 20 μg/kg appears to be optimal for this anaesthetic technique as it abolishes the pressor and heart rate responses to tracheal intubation without causing undue hypotension or bradycardia. In addition, early intubation at one minute after vecuronium is greatly facilitated with good or adequate conditions in all patients and no coughing or straining after intubation. In the light of the recent finding of dissociation between intra-ocular pressure and systemic blood pressure changes with this type of anaesthetic technique,[1] we are currently investigating the ability of alfentanil to attenuate the intra-ocular pressure rise with intubation.

Acknowledgments

We would like to thank Dr P.S. Baines and Dr S. Roxburgh for allowing us to study patients under their care, Mr J. Kilcullin for skilled assistance, Critikon for the use of a Dinamap 1846 automatic blood pressure recorder and Ms A. Formica for skilled secretarial help.

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Harold Randall Griffith, OC, MM, MD, CM, FRCPC, FFARCS—an appreciation

One of the most outstanding anaesthetists of this century, Dr Harold Griffith died in May 1985 at the age of 90 years. A full obituary was published in the *Canadian Anaesthetists' Society Journal*, 1985; 4, but it is fitting that the death of such a disti international figure in our specialty should b

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in *Anaesthesia*. His contribution to anaesthesia reads like a history of the specialty during the period of its most rapid development.

From the time of his first appointment as specialist in Montreal in 1923, he exhibited his original thinking by adopting ethylene gas in preference to the conventional nitrous oxide and continued to use it until the introduction of cyclopropane by his friend Dr Ralph Waters in 1933, a subject on which he wrote extensively. His name is famous to all for the introduction of curare into anaesthetic practice in 1943. In the same year his innovative mind established the first postoperative recovery room, now an accepted feature of all operating suites. In that same year the Canadian Anaesthetists' Society elected him its first President. He soon joined Dr Wesley Bourne in founding one of the first academic departments of anaesthesia in North America, at McGill University.

Not content with his contribution to the establishment of anaesthesia as a recognised specialty in North America, he proposed to extend this recognition world wide. In 1948 he was elected President of the International Anesthesia Research Society, of which he had been a member since its inception in 1922, and in 1951 this Society held its first overseas meeting in Europe. This attracted a large gathering of interested medical practitioners from many countries. Papers and exhibits were presented at the Salpetrière Hospital in Paris in September of that year.

Many of those interested in promoting anaesthesia at this time were surgeons; such eminent persons as Professor Dogliotti of Italy, author of the then standard work on local and regional anaesthesia and Professor P. Monod, an eminent Paris surgeon, were present. I was fortunate to attend in company with the late Professor Ronald Woomer, who was, that year, Director of the WHO School of Anaesthesia in Copenhagen and the late Dr Bryn Thomas and a number of other colleagues from Britain. During the course of the congress it appeared that a world organisation for anaesthesia was being considered which would include surgeons, with the possibility that they might even control the organisation. It may be difficult for colleagues today to appreciate that anaesthetists were at that time still beholden to surgeons for their livelihood. In the event it was with considerable relief that we understood that it had been agreed that the proposed world society should be exclusively for anaesthetists. I have no doubt that this decision was largely brought about by the commanding and persuasive personality of Dr Harold Griffith. Had the decision gone the other way, the subsequent history of the World Federation of Societies of Anaesthesiologists would have been very different.

Dr Griffith was inaugurated as the first President of the World Federation at Scheveningen, The Netherlands, in 1955. He was given the Hickman Medal of the Royal Society of Medicine in 1956 and, at the second meeting of the WFSA in Toronto in 1959, he was designated Founder President.

From the time of his winning the Military Medal as a stretcher-bearer in France in 1916 to his election to the Order of Canada in 1974, this remarkable man devoted his life to the advancement of medical practice; the specialty of anaesthesia will owe him a debt of gratitude in perpetuity.

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Cardiovascular response to intubation

This letter refers to an article by Dr Boralessa and his colleagues (*Anaesthesia* 1983; **38**: 623–7). The authors compared the cardiovascular responses to intubation after thiopentone or midazolam. Both groups of patients received pancuronium which was given after the loss of eyelash reflex following each induction agent. Tracheal intubation was performed 3 minutes later.

It seems unreasonable to compare the cardiovascular responses to intubation between the groups in this study, because by the end of 3 minutes following the loss of eyelash reflex, the level of anaesthesia in patients who had thiopentone would be much lighter than those who received midazolam. The tracheal intubation was thus performed at two *different* levels of anaesthesia. The observed increase in cardiovascular variables in patients who received thiopentone may partly be due to this fact. Midazolam takes up to 3 minutes or longer to exert its maximum effect.[1]

It has been well documented that the degree of cardiovascular aberation following tracheal intubation depends on the level of anaesthesia and several techniques have been advocated to obtund this response.[2,3] On the basis of their paper it cannot, therefore, be said that midazolam is a superior agent with regard to the cardiovascular aberations following tracheal intubation as compared to thiopentone.

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Anaesthesia for extracorporeal shock wave lithotripsy

We were interested in the correspondence on the above subject (*Anaesthesia* 1986; **41**: 429–30) having now anaesthetised 650 patients (including 22 children) for the above procedure (ESWL). We agree with Dr Pennant about the need for great care when the arms of anaesthetised patients are positioned, since one of our patients sustained signs of brachial plexus stretch injury which persisted for 6 weeks. It is important that the height of the arm support is not too great and that the upper arm is not abducted *and* externally rotated.

In a series of 100 patients randomly allocated into two equal groups and ventilated with N_2O and O_2 (33%) either by intermittent positive pressure ventilation (IPPV) or by high frequency jet ventilation (HFJV) we found, in the latter group, that blood gases were unsatisfactory ($P\text{aco}_2 < 6.3$ kPa and $P\text{ao}_2 > 11.2$ kPa) in 17 patients, mainly in the heavier males. There was no statistical difference in the mean number of shocks delivered to the two groups, although the total mean X ray exposure time was significantly less in the HFJV group (316 and 250 seconds).

In a further 40 patients ventilated by IPPV it was found that, using the Servo ventilator 900C and the Servo lung mechanics calculator 940, there was a 32% rise in peak airway pressure and a 36% fall in lung compliance as a result of positioning, immersion and during the course of treatment. We believe that these manoeuvres, which are an integral part of ESWL, produce a reduction in lung volumes and that these changes, which presumably also occurred during HFJV, led to the unsatisfactory blood gas status in a third of these patients. We have therefore abandoned the use of HFJV during anaesthesia for ESWL and now use IPPV with low frequency and low tidal volume, monitoring end-tidal CO_2 concentration and arterial oxygen saturation cutaneous oximetry. This technique avoids the need for invasive arterial cannulation and allows easy targetting of the calculus. Together with our learning experience the average X ray exposure time is now 150 seconds.

In a series of 100 patients we found that there was a 30% reduction in mean arterial blood pressure on positioning the patient in the stretcher. Immersion in the warm water bath did not result in any further fall in mean arterial pressure. Rather it tended to rise, presumably because of the hydrostatic compression effect of immersion. In six patients in whom central circulatory variables were measured using a pulmonary arterial catheter, it was found that right atrial pressure increased 2.5 times, pulmonary capillary wedge pressure doubled, pulmonary vascular resistance increased by 31% and total peripheral vascular resistance increased by 22%. These changes are of the same order of magnitude as those reported by Weber *et al.*[1]

Our practice is to administer frusemide 20 mg as soon as the calculus is located by X ray screening, together with 1000–1500 ml of intravenous fluid during the treatment; this takes an average time of 36 minutes. The initial rate of fluid administration is guided by the degree of fall in mean arterial pressure on positioning, and its subsequent rise on immersion, particularly in hypertensive patients.

In the paper by Abbott, Samuel and Webb (*Anaesthesia* 1985; **40**: 1065–72) the authors comment that patients lose heat. In a series of 100 patients we found that the mean oesophageal temperature before immersion was 36.1 (SD 0.6) °C and that on extraction from the bath after an immersion time of 36.1 (SD 15.4) minutes it was 36.2 (SD 0.6) °C. Some patients (45) gained heat by up to 1.5 °C and some (42) lost it by up to 2 °C. Of the 33 patients who were immersed between 40 and 80 minutes, only 16 lost heat. Shivering was not a problem in these patients.

Another interesting finding was the observation of gastric and duodenal erosions in 32 of a series of 40 patients who were gastroscoped. This was done because it was noticed that many patients regurgitated on extubation and others had gastric dilatation on the post-ESWL plain X ray and we thought that the shock waves may have been exerting some effect on the stomach. This appeared to be the case, but there has been no significant morbidity from this effect.

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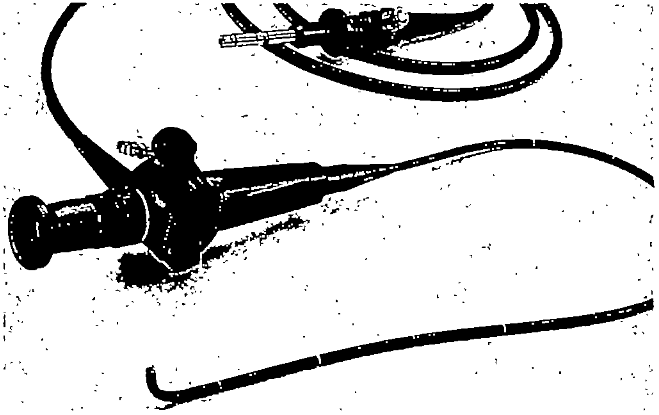

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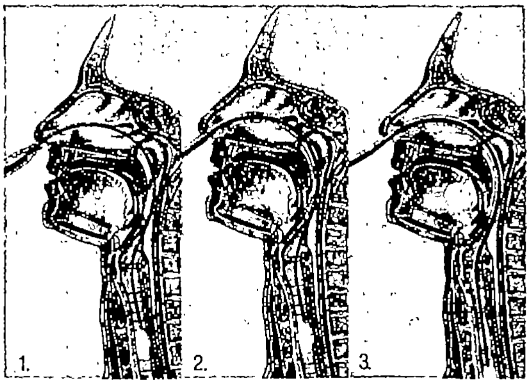

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★ 1. Fiberoptic bronchoscopy for anaesthesia. Watson, C.B., Anaesthesiology Review (1982), IX: 17-25.
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Facial paraesthesia and propofol

There is an interesting phenomenon that I have observed during intravenous induction of anaesthesia with propofol (Diprivan). Thirty-two consecutive adult unpremedicated daycare patients who were undergoing minor surgical procedures were induced with propofol 2.0–2.5 mg/kg injected over 20 seconds via a butterfly needle in the forearm. Thirteen patients reported facial sensations of either burning, numbness or tingling before they fell asleep. All 32 patients were seen postoperatively and the same 13 patients confirmed their experience of facial paraesthesiae during the induction.

One study included the report that 3% of patients had a tingling sensation at the site of injection,[1] and another report[2] found an incidence of 5% who experienced facial tingling. However, none of them mention the alternative sensations of burning (six patients) and numbness (two patients) and the remaining five patients reported facial tingling. In this small series of patients, 40% experienced facial paraesthesiae, a higher proportion than previously reported. Using the Chi square test $p > 0.001$, so this difference is unlikely to be due to chance.

It is impossible to ascribe the paraesthesiae to either the propofol or its emulsion, or the combination of the two. It should be noted that the emulsion agent, a soya bean oil extract, is similar to that used in Intralipid and the diazepam formulation Diazemuls. No reaction of a similar nature has been reported, although it must be borne in mind that a larger quantity of emulsion is injected rapidly during induction with propofol.

I have no explanation why the paraesthesiae should be centred on the face, nor whether the mechanism is a central or peripheral neural manifestation.

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Safety of a new system for continuous positive airway pressure

The use of continuous positive airway pressure (CPAP) is well established in children, but its use in adults is more controversial.[1] One factor that has slowed the increasing popularity of CPAP in adults is the difficulty in designing a satisfactory system; the ideal CPAP system maintains a constant pressure throughout the respiratory cycle. There are two types of CPAP system: either a high flow (approximately 30 litres/minute) open system with a large compliant inspiratory reservoir,[2] or a demand valve system. The former type is often cumbersome, while the latter may increase the work of breathing.[3,4] A modification of the high flow open system has recently become available in this country (Downs' CPAP System, Medic-Aid Ltd.). The essence of this new system is the Downs' CPAP Flow Generator. This is an air-entraining venturi device, which plugs directly into a piped oxygen wall outlet, giving flows of approximately 100 litres/minute.[5] There are controls to adjust the flow and the inspired oxygen concentration/$\mathrm{IO_2}$(F). The gases are passed through a humidifier and to the patient via a T-piece; on the expiratory limb is a single use CPAP/PEEP valve (pre-set at 0.25, 0.5, 0.75, 1.0. 1.25, 1.5 or 2.0 kPa).

There was recently in this hospital an instance of a CPAP/PEEP valve which jammed after repeated use of this new system. There is neither a pressure relief valve nor a reservoir bag to act as a pressure limiting device within the system, so it appeared that the patient might have been exposed to pipeline pressure (410 kPa). However, since this was obviously not the case, and the gases were vented through the venturi device, we decided to investigate the safety of the system.

The system was set up as for normal use, without a humidifier, but with an oxygen analyser (Oxycheck, Critikon) in the system and a dry gas meter (Parkinson Cowan) on the expiratory port of the CPAP valve. A mercury column was attached to the patient end of the T-piece. The expiratory port of the CPAP valve was occluded and the pressure measured. This was repeated over a wide range of $\mathrm{F_{IO_2}}$ and flow rates. The occlusion pressures were highest (5.3–6.4 kPa, mean 5.8 kPa) when the flow was set at maximum (126–152 litres/minute, mean 135 litres/minute). The occlusion pressures appeared to be independent of the $\mathrm{F_{IO_2}}$ at maximum flows.

We have shown that the maximum pressures that can be generated within this new CPAP system are of the same order as the opening pressures of the pressure relief valves found within most anaesthetic or intensive care breathing systems. The wider use of this system can therefore be safely recommended.

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A matter of vigilance

In his editorial (*Anaesthesia* 1986; **41**: 129–30) Dr R. A. Green reminds us of the steady incidence of totally avoidable anaesthetic-related deaths and can there be any doubt that these form the tip of an iceberg of largely undocumented near-misses?

The call for greater vigilance in the operating theatre draws me to compare British practice with my current North American experience. Here such a call would be replaced by one for a new monitoring standard. In this hospital we use only modern anaesthetic machines, which incorporate alarm systems for gas supply, power supply (with battery back-up) and low oxygen gas mixture. The integral bag-in-bottle ventilator is equipped with high and low pressure alarms. To this is added a mass spectrometer terminal, providing complete analysis of inhaled and exhaled gases and equipped with alarms for any out of normal range value. Next comes a separate fuel cell type oxygen analyser with alarms. Then we have an automatic cuff blood pressure machine and a datascope for ECG, intravascular pressures and temperature, both equipped with alarms. In the case of concern over oxygenation, there are several pulse oximeters to share between the nineteen otherwise similarly equipped theatres. On top of all this, it is accepted practice, during all anaesthetics and at all times, to monitor the breath and heart sounds through an oesophageal or precordial stethoscope; in some States this is mandatory.

Expensive this certainly is, but is it good clinical practice? Undue reliance does sometimes seem to be placed on the monitoring equipment and numerical data pertaining to the patient, while very little emphasis at all is placed on *clinical* assessment. This you will agree is detrimental to patient care and is, incidentally, also wasteful of money. There are however benefits and one of these is a dramatic reduction in the incidence of simple mistakes of the type which result in many of the anaesthesia-related deaths in Great Britain. Disconnexions, faulty oxygen delivery and so forth simply cannot go unnoticed. These mishaps are usually the consequence of human error and, as such, are very hard to eliminate completely from anaesthesia, especially when basic and sometimes poorly designed equipment is kept in service when long overdue for replacement.

The excessive and expensive approach adopted here has been forced by enormous malpractice settlements awarded to a litigious society and here it can be seen as directly cost effective. By the same token the approach also works; it does make anaesthesia safer. Perhaps in Great Britain we should change a little in this direction before it is forced upon us.

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Non-vagolytic anaesthetic sequence and sinus arrest

Correspondence continues on the problem of bradycardia and asystole following anaesthetic induction sequences involving the clean neuromuscular blockers, atracurium and vecuronium.[1–5] A resurgence of interest in suxamethonium mediated bradydysrhythmias and asystole,[6–8] in several centres, including this one has prompted us to comment on the two cases reported by Dr Higgins and Dr Thorp (*Anaesthesia* 1986; **41**: 89–90).

Case number 1 developed bradycardia and sinus arrest 15 minutes after any intravenous drugs. Pethidine and promethazine, which both have vagolytic properties, were given as premedication, as was the sympathomimetic aminophylline. The inspired concentration of halothane is not reported, nor is there any assurance that ventilation was adequate. Before the cardiac dysrhythmia is finally attributed to vecuronium, we would want to rule out overdose of halothane or hypoventilation.

In case number 2, was a second-dose effect from suxamethonium excluded? It is common practice in Britain to use intravenous cannulae of the Venflon type (with a Luer injection port integral to the device). These cannulae have a port deadspace of approximately 0.1 ml. If this form of intravenous access was employed, and standard strength (50 mg/ml) suxamethonium used then a second dose of 5 mg of the drug may have been administered inadvertently at the time of injection of the incriminated vecuronium.

Next, we infer from the letter of Higgins and Thorp that in neither case was ECG monitoring employed during induction of anaesthesia. Our own observations and those of Sorensen *et al.*[8] on asystole and extreme bradycardia following a single dose of suxamethonium probably would have been missed if continuous ECG monitoring had not been started before induction. The lack of reports of this phenomenon from the UK is possibly due to the British practice of transferring anaesthetised patients from the induction room to the operating room before ECG monitoring is started. Many such dysrhythmias may therefore go unnoticed, with the patient developing an escape rhythm and spontaneous return of normal electromechanical activity. Dr Higgins and Dr Thorp point out, and we have observed, that the patients maintain normal colour, so there is no reason to suspect a problem.

We would strongly argue the case for the clean neuromuscular blockers. Developments by the pharmaceutical companies in the last decade have provided anaesthetists with potent, reliable and specific drugs. Surely we must learn to do without side effects which vary greatly in their intensity and duration. If we desire vagolysis, then why not use a vagolytic, particularly if future developments allow the pre-induction identification of the individual who is susceptible to vagal overdrive?

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Diamorphine

Dr Reynolds (*Anaesthesia* 1986; **41**: 554) avers that the breakdown of diamorphine is well-known to take place in aqueous solution at room temperature and amusingly suggests that we are giving morphine, not diamorphine, in our technique of continuous diamorphine infusion for postoperative pain prevention.

However, reference to the Pharmaceutical Codex[1] reveals that this breakdown is a very slow process; 10% of a diamorphine solution, pH 4.0, maintained at 25 °C is so affected over a 5-day period. Recently, a much longer storage period has been investigated by workers who examined the rate of breakdown of diamorphine solution over 2 weeks.[2] High pressure liquid chromatography failed to reveal significant breakdown.

We change our syringes every 24 hours for convenience as well as on grounds of sterility. Thus, though we did not investigate this aspect of our management, nor claim to, according to current knowledge and contrary to Dr Reynolds' assertion, it seems that significant changes do not occur within such a time span.

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Caudal epidurals—a further caution

A 49-year-old lady was admitted for a caudal epidural to manage chronic low back pain and left-sided sciatica. Ten months previously she had had a chymopapaine discolysis at L_5–S_1 level which had failed to relieve her symptoms. The only other salient points in her history and examination were mild angina on exertion, with a normal resting ECG and no current or previous therapy; she was moderately obese. Straight leg raising (SLR) was 70° on both sides.

No premedication was ordered and she was brought to the theatre where her supine arterial blood pressure was 120/70 mmHg. A 2.0-mm intravenous cannula was inserted under local anaesthetic on the dorsum of the left hand and a fast-running infusion of normal saline was commenced. The patient was turned onto her left side, the sacral hiatus was identified and 2% lignocaine was infiltrated to superficial and deep layers. After 750 ml of crystalloid had been infused intravenously, the caudal epidural space was identified by loss of resistance to air. Forty millilitres of 0.25% plain bupivacaine with 80 mg of depomedrone was then injected rapidly through a 19-G needle. The patient was returned to the supine position with her head on one pillow. This large volume rapid injection is deemed necessary to divide suspected adhesions in the lumbar region.

Over the next 20 minutes the patient received a total of 2 litres of crystalloid and her blood pressure remained steady at 110/60 mmHg. The only apparent effect on the patient was mild paraesthesia of the lower legs and feet. During the 30 minutes following the injection SLR was demonstrated on six occasions in each leg and had improved to 90° on the right and to 85° on the left.

Quite without warning, when the patient was about to be returned to the ward, she complained of nausea, sweating and a great heaviness in her chest. The systolic blood pressure was found to be 60 mmHg and a sensory deficit to pinprick to T_2 was found. Breathing was diaphragmatic.

The infusion was speeded and polygeline 1500 ml was given with a further 3 litres of crystalloid solution. Over the next 30 minutes the blood pressure returned steadily to the pre-operative value. After one hour of rapid intravenous fluids, a urinary catheter was passed and a residual of 1400 ml urine was drained. The patient had had no desire to micturate. Muscle tone returned over the next 2 hours and the patient was returned to the ward.

The case is interesting on two accounts. Firstly, the sudden delayed spread of local anaesthetic up the epidural space and, secondly, the degree of motor blockage caused by 0.25% bupivacaine. There are several observations to be made about this case. The spread up the epidural space may be increased in speed and extent by a pumping effect of excessive demonstration of straight leg raising too soon after the injection. Perhaps a period of 30 minutes should be allowed to elapse, to allow all the local anaesthetic to bind to the tissues. The procedure, often carried out by the orthopaedic department without anaesthetic presence, should be treated with the same respect as, for example, Bier's block. The patient should remain in the recovery room until micturition has occurred and blood pressure should be monitored by appropriate staff. The use of a shorter-acting, and perhaps less toxic, local anaesthetic agent should be considered.

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A rare cause of unexpected difficult intubation

A 39-year-old healthy man recently presented for a routine haemorrhoidectomy under general anaesthesia. The pre-operative examination was uneventful. Anaesthesia was induced with 1.5 mg alfentanil after pre-oxygenation for about 3 minutes with 100% oxygen; this was followed by 275 mg of thiopentone. Suxamethonium (80 mg) was injected after loss of consciousness, and intubation was attempted after one minute by direct laryngoscopy. Neither the epiglottis nor the vocal cords could be visualized. Instead, there was a smooth, spherical, tumour about 3 cm in diameter, right at the base of the tongue, which seemed to arise from the vallecula. Attempts were made to pass the tracheal tube with a malleable introducer, behind the tumour, keeping it well anterior up against the tumour. Intubation was successful at the third attempt. Further anaesthesia was uneventful.

A postoperative referral to the ENT department was made. On direct questioning the patient did admit to the occasional feeling of a lump in his throat. Indirect laryngoscopy showed a round, smooth, yellowish tumour in the vallecula. It was concluded that the patient had a small lipoma of the vallecula and suggested that no active treatment was necessary, since the patient had no symptoms.

A symptomless lipoma of the vallecula is a fairly rare condition to cause a difficult intubation. The above case also suggests that the patient's history or appearance does not necessarily warn of an impending difficult intubation. A reliable forecast is not always possible.

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Difficult intubation—forwarned is forearmed

The report of a case of unexpected difficult intubation from Drs Nathan, Scott and Mohandas (*Anaesthesia* 1986; **41**; 664–5) states that there was no record of any problems with anaesthesia, although the patient had previously undergone surgery usually requiring intubation. It is quite possible that difficulty was indeed encountered at those times, but that no record was made.

When any difficulty with anaesthesia is encountered, particularly with airway management or intubation, a detailed and conspicuous record should be made in the patient's notes. The patient should also be informed of the problem at a suitable time postoperatively, and reassured that future anaesthesia is not precluded.

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Epidural test doses in obstetrics—let us face facts

The physical principles test, as compared to the pharmacological effects of a local anaesthetic, is stated to be quicker and more reliable in determining correct placement of plastic tubing in the epidural space.[1] This test depends primarily on the lumen of the plastic tubing being unobstructed after its placement, so that it can act as a manometer. However, if kinking (acute bend) occurs in the plastic tubing, the tubing can have a ball valve effect. Therefore, air or fluid injected into the tubing can pass the kink and exit from the tubing. However, the kink may not allow air and/or fluid to pass in the opposite direction; this precludes it from refluxing into the plastic tubing and acting as a manometer. Evidently, in such a situation, although not stated by Shah, the tubing is withdrawn even though it may be correctly placed in the epidural space. On the other hand, when a ball valve effect occurs, the pharmacological results of an effective test dose can be properly monitored and this avoids withdrawal of kinked plastic tubing which is, after all, in the epidural space.

In the long run, the pharmacological test is quicker because the time to withdraw and re-insert the tubing is not required. In addition, the pharmacological test solution which I use, namely 0.015 mg of adrenaline, which within 45 seconds indicates an intravascular injection and a milligram dose of a local anaesthetic which within 2 minutes results in evidence of spinal block,[2] does not require another person to compress the jugular veins,[1] which may cause discomfort. Furthermore, it is equally, or even more reliable. Since its routine use in 1979, I have had no systemic toxic reactions, high or total spinal blocks in over 5000 surgical or obstetrical epidural blocks while teaching residents. Prior to then, in every 2000 epidural blocks, 3–4 convulsions or one total spinal block resulted. Neither has fetal depression as demonstrated by the cardiotacograph been observed from 0.015 mg of adrenaline and if it is administered immediately after a uterine contraction it has always signalled intravascular placement of the needle's bevel or the end of the plastic tubing.

To conclude, of various tests to rule out an intravascular or subarachnoid injection using a single test dose, the pharmacological effects of a local anaesthetic with adrenaline is safe and still the most reliable. Although in disagreement with Prince and McGregor[3] if administered as advised,[2] perhaps it is even foolproof.

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Adrenaline and acute anaphylactoid reactions

The case report by Harrison (*Anaesthesia* 1986; **41**: 600–3) describes anaphylactoid reactions to precurarising doses of gallamine and provides an interesting discussion on the mechanism of such reactions. However, I feel that their management of the resultant cardiovascular collapse needs further comment.

Two cases of anaphylactoid cardiovascular collapse were described. Both patients became profoundly hypotensive. However, the first patient received only one litre of saline, the second was treated with steroids, chlorpheniramine and terbutaline but no fluids, despite requiring external cardiac massage. Adrenaline was withheld due to the presence of tachycardia and apparent vasoconstriction.

The pathophysiology of anaphylactoid reactions is well described. Cardiovascular collapse follows histamine-induced vasodilatation and increased capillary permeability. Changes in the haemoglobin concentration noted during severe reactions suggest that plasma losses may exceed 35% of the blood volume within the first 10 minutes.[1] Histamine does have some action on heart muscle *in vitro*, but the tachycardia accompanying anaphylactoid reactions is probably secondary to endogenous catecholamine release and, as such, is relatively benign.[2] In view of these pathophysiological changes, the omission of adrenaline and adequate fluid therapy in the two cases described may well account for the rather protracted hypotension.

It is clearly impossible to undertake controlled clinical trials of therapy in acute anaphylaxis. However, information from large retrospective studies can provide useful data on the safety and efficacy of a particular therapy. Fisher reviewed 227 episodes of anaphylactoid cardiovascular collapse which occurred over a 10-year period.[3]

Adrenaline was the most effective inotrope if used as first line therapy. When administered to 142 patients, only two required a second sympathomimetic. Ventricular fibrillation occurred in four patients. However, all four patients had received bolus doses of adrenaline during a halothane anaesthetic. The same study could find no evidence of any immediate response to steroids or H_1 antihistamines.

Adrenaline, in conjunction with adequate fluid therapy, is a safe and effective first line treatment for anaphylactoid cardiovascular collapse and need not be omitted in the presence of tachycardia or apparent vasoconstriction. It is interesting to note that all six of the patients who died in Fisher's series received adrenaline only late in the course of resuscitation.

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Anaphylaxis and precurarisation

The case report by Dr Harrison and Dr Bird (*Anaesthesia* 1986); **41**: 600–4) was interesting as for many years I have used 30 mg gallamine triethiodide prior to suxamethonium. Recently, anaesthesia was induced in a 38-year-old woman, for laparoscopic sterilisation, with thiopentone 450 mg, gallamine 30 mg and suxamethonium 100 mg. There was moderate bronchospasm almost immediately and skin flushing over the whole body, with complete circulatory failure. Resuscitation included brief external cardiac compression, 600 mg hydrocortisone, an infusion of dextrose 4% in saline 0.18% and two units of human albumen. Good oxygenation was maintained throughout, spontaneous ventilation was present after 5 minutes and full consciousness after one hour. A stable arterial blood pressure of 110 mmHg systolic was not achieved for 2 hours, but thereafter recovery was uneventful.

This case has been reported to the Committee on Safety of Medicines. Dr J. Watkins kindly carried out late blood tests and my local colleague, Dr E. Potts carried out skin tests. The latter showed strong positive results for both gallamine and suxamethonium.

The comment in the article quoted, that 'outcome of cardiovascular collapse is invariably good' is unacceptable. A great number of patients may have been spared suxamethonium pains, but I consider that the technique discussed is no longer justified, and anticipate the advent of a similar drug to suxamethonium but without its complications.

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An ideal agent for drawover anaesthesia?

The paper by Hollis (*Anaesthesia* 1986; **41**: 309–15) was extremely interesting. It does seem a good idea to mix halothane and trichloroethylene when a single vaporizer is all that is available for drawover anaesthesia, particularly when cost is a consideration. However, the difficulty in providing high concentrations after approximately 10 minutes of anaesthesia and the impossibility of varying the volatile agent concentrations independently according to clinical requirements, does limit the versatility of this technique. In addition, the apparent increase of the trichloroethylene concentration with increasing duration of anaesthesia is the reverse of clinical requirements and might be expected to result in delayed recovery.

Hollis makes no mention of isoflurane in his opening discussion on the volatile agents now available for single agent drawover anaesthesia. The characteristics of this agent suggest that it would be suitable for use with this technique. Isoflurane is nonflammable, not explosive, chemically stable and has a low rubber solubility.[1] Induction and recovery are rapid, the cardiovascular system is stable and there is little respiratory depression.[2,3] Isoflurane also has some analgesic properties[4] and biotransformation is minimal,[5] making it suitable for the repeat anaesthesia that is almost always required in the military setting.[6] The technique which uses the Triservice anaesthetic apparatus,[7] but with one vaporizer, could become more exportable.

It is therefore suggested that in view of the above advantageous properties, isoflurane would be a more suitable agent for use with a single vaporizer than would a mixture of halothane and trichloroethylene, provided one can afford it.

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A reply

Thank you for allowing me to reply to Dr Tighe's letter. Yes, the technique has several disadvantages compared to using two vaporizers at once. However, in my experience, (albeit limited to a few tens of cases), the theoretical difficulties are not a practical problem. Dr Tighe cites the difficulty of providing high concentrations after 10 minutes. Although this appears so from the vapour output graph, this was worked out with a continuous sine wave airflow of 5 litres/minute which is greater than the minute volume of a typical patient, so, in practice, is less and the vapour output does not fall off as fast as shown on the graph.

Once a small dose of thiopentone was necessary to improve anaesthesia rapidly, but this could have been avoided with a little patience. Alternatively, a small dose of fentanyl or gallamine would have been satisfactory. The suggestion that the trichloroethylene concentration rises with time and may cause delayed recovery is not borne out by my own experience. The trichloroethylene concentration only increases by about 0.25% at a given setting over an hour. The important thing is that the halothane output follows the shape of the uptake curve of an inhalational anaesthetic. Lowering the vaporizer setting rapidly lowers the inspired halothane concentration so that the overall depth of anaesthesia soon decreases and recovery need not be prolonged.

With respect to isoflurane for drawover anaesthesia in spontaneously breathing patients, I await with interest the results of studies on this subject; however, in a closed system, with oxygen alone, in patients premedicated with opiates (a situation akin to drawover where N_2O is not used) extreme respiratory depression often occurs although it improves when surgery starts. This makes the need for additional oxygen almost essential. The establishment of mask anaesthesia with isoflurane without nitrous oxide may require more skill than with halothane/trichloroethylene because of its pungency.

The mixture halothane and trichloroethylene is of limited use and something of an anaesthetic curio. The study was initially undertaken simply to satisfy my own interest in a problem to which nobody seemed to know the answer. The fact that the mixture works as a reasonable anaesthetic is something of a bonus. One aspect which I had not considered earlier was its application in veterinary anaesthesia where the use of N_2O is restricted (MAC in most mammals, other than man, is about 200%) and it is hazardous in herbivores because of the huge quantities of gas in their gut, which can lead to severe respiratory difficulty when it is used.

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Pre-operative visit

The patient who is about to undergo an operation will always benefit from a pre-operative visit. It is therefore somewhat disturbing to read in a recent journal[1] that the practice of pre-operative assessment by an anaesthetist is by no means universal and, further, it is not infrequently carried out by proxy. The situation is, however, dictated by physical considerations not always under the anaesthetists' control. For example, some consultants have commitments to several hospitals. Operation lists for the next day, especially for the morning, are not available until towards the end of the previous afternoon and it is manifestly impracticable to expect anaesthetists to make additional visits to other hospitals after completing their usual list. Of course things would be better if surgeons could be persuaded to produce lists earlier. But rapid turnover of surgical patients can be achieved only if patients for the next day's list are admitted to the hospital in the middle of the morning before operation—and even then the junior surgical staff are unlikely to be able to sort them out until the afternoon.

It would therefore seem that there is no easy solution to the problem, unless perhaps those who draw up job descriptions do so in such a way as to minimise the number of hospitals an anaesthetist must visit. Ideally, he should be appointed to one institution, but except in the largest hospitals this is not possible.

The training of registrars and other members of the junior staff demands that they be allocated to lists where they may receive training. This too can limit their ability to make pre-operative visits if they have to work in more than one hospital. The obvious solution is to allocate each registrar to one unit for a block period of study for a month at a time. But it is the experience of those who have attempted to do so that such rigid training schedules sooner or later break down, usually because someone falls ill or is absent for some other reason.

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Paradoxical air embolism during hip surgery?

We read with interest the paper by D.G. Clayton *et al.* (*Anaesthesia* 1985; **40**: 981–9) in which it was suggested that paradoxical air embolism was responsible for cardiovascular and neurological complications which they described in four neurosurgical cases. They commented that while venous air embolism was common in the sitting position during neurosurgery, only a small proportion of patients suffered serious sequelae and they postulated that paradoxical embolisation was responsible for these.

Venous air embolism is also common in hip surgery involving cement[1,2] and while such surgery is generally considered to be safe, serious complications undoubtedly occur.[3] Transient hypotension is not uncommon[4] and air embolism seems a likely precipitating event. Is it possible that some of the more serious complications reflect paradoxical embolisation? If this is so, one might expect electrocardiographic changes from coronary embolism, which would occur before hypotension was observed and there might be neurological sequelae, from cerebral embolism without gross hypotension.

It is interesting to note that the patient undergoing hip surgery, reported in 1970 by Hyland and Robins, showed, at post mortem examination, 'air and fat in the pelvic veins on the same side as surgery, in the right heart and in the coronary vessels'.[5]

Clayton *et al.* describe various ways in which it is thought that air might pass from right to left sides of the heart and they discuss the role of posture and intermittent positive pressure ventilation (IPPV). IPPV is often used in hip surgery. Do patients undergoing such surgery lying on their left side fare better than patients lying on their right?

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A reply

Dr Young and Dr Wright raise some interesting points regarding air embolism associated with hip surgery. Michel[1] reported a 30% incidence of air embolism during this procedure, with an increased incidence during spontaneous compared with controlled ventilation. Air embolism is clearly an important factor in causing hypotension at the time of placement of the femoral component.

They ask if paradoxical air embolism is likely to occur in this situation. For this to be a possibility, right atrial pressure must be higher than left atrial pressure. The population of patients undergoing hip replacement are elderly and thus a proportion are likely to have an element of right heart failure secondary to pulmonary disease or ischaemic heart disease. These patients may have high right atrial pressures. Secondly, when air embolism occurs, air entering the pulmonary circulation causes pulmonary hypertension and right atrial pressure to rise. In these circumstances, the conditions necessary for paradoxical air embolism occur. The case reported by Hyland and Robins,[2] where air was found at post mortem in the left coronary artery, is clearly a case where paradoxical air embolism occurred.

The amounts of air involved in air embolus during hip surgery are normally small, as only a limited amount of air is contained within the femoral shaft. Anderson,[3] reporting a series of patients with air embolism in this situation, was only able to aspirate a maximum of 3 ml of air from the right atrium. Where small amounts of air cause profound cardiovascular collapse, it is our contention that this may represent paradoxical air embolism, with the likelihood of air having entered the coronary circulation.

In their classical experiments, Durant *et al.*[4] showed that dogs could tolerate air embolism better when lying on their left sides. They suggested that with the dogs on their left sides, the pulmonary outflow tract assumed a position inferior to the body of the right ventricle and air tended to be churned into a froth in the right ventricle and was transported into the lungs and excreted. Whether this work in dogs can be extrapolated to man is open to doubt because of anatomical differences. Secondly, as very small bubbles of air such as those contained in froth, may pass through the pulmonary circulation, particularly if patients are receiving aminophylline, it is not certain whether the left lateral position would protect against paradoxical air embolism by the transpulmonary route. Thus, although the left lateral position may offer theoretical advantages, we are not aware of any work which confirms this view on paradoxical air embolism in man.

Paradoxical air embolism is certainly a possibility during hip surgery. How often it actually occurs is difficult to predict. ECG monitoring should certainly be mandatory during hip surgery. Whether the other diagnostic tools one uses during anaesthesia in the sitting position should also be used is questionable at the moment. This sounds like an interesting research project for someone.[1]

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Two percent lignocaine spinal anaesthesia

The choice of agents for spinal anaesthesia in the United Kingdom remains limited with the loss of cinchocaine and the advent of bupivacaine. There are clinical situations where spinal anaesthesia may be the technique of choice, but where prolonged motor and sensory blockade is inappropriate.

Five percent hyperbaric lignocaine has been available since 1952, but the preparation is not widely marketed in the UK. It provides rapid and effective spinal anaesthesia, but the reasons for the use of the higher concentration, as compared with equivalent concentrations of other local anaesthetic agents, are not clear. Isobaric 2% lignocaine is readily available in ampoules. It contains lignocaine hydrochloride (20 mg/ml), sodium chloride (6 mg/ml) with sodium hydroxide to buffer to pH 6.9, in sterile water. There are no antioxidant or antimicrobial additives.

The usefulness of isobaric 2% lignocaine is not widely appreciated, but it gives rapid and consistent analgesia in doses ranging from 20–80 mg, with durations of 55 minutes (SD 7.1) to 143 minutes (SD 29), respectively.[1] In a further series of 20 patients, 2 ml of isobaric 2% lignocaine (40 mg) was injected intrathecally at the L_3–L_4 interspace for urological and lower limb orthopaedic procedures. The latency period was 5 minutes or less, the mean extent of sensory block was T_8 (range T_6–T_{10}) and the mean duration to return of motor function was 62 minutes (range 45–85). Supplementary anaesthetic drugs were not required in any patient.

Although an old drug, lignocaine at the 2% concentration is not commonly employed as a spinal anaesthetic. It merits consideration as an effective technique where prolonged spinal anaesthesia is not indicated.

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SAG-M Blood

Many anaesthetists will be aware that SAG-M blood may now be supplied for transfusion. This blood product contains packed red cells diluted with 100 ml saline–adenine–glucose–mannitol solution; most of the plasma proteins are removed during preparation. When patients require massive transfusion, blood banks normally supply whole blood, but may now be forced to issue SAG-M blood if there is a heavy demand. We would like to report two cases in which we feel that SAG-M blood contributed to clinical problems.

Case 1 A 71-year-old man presented with severe back pain and hypotension due to a ruptured aortic aneurysm. Aortic repair was technically successful, but he required 24 units of blood, of which the last ten were SAG-M cells. Despite four units of fresh frozen plasma and twelve units of platelets, no clots were seen during the latter part of the procedure and the patient died from uncontrollable haemorrhage.

Case 2 A 75-year-old man also presented in shock from a ruptured aortic aneurysm. Once again surgery was technically successful, although 28 units of blood were required, of which ten were SAG-M. This patient subsequently developed massive fluid overload and renal failure. Seven litres of fluid were removed by haemofiltration, but the patient died on the second postoperative day from cardiac failure.

It was our impression that both these patients showed a clinical picture that differed from similarly ill patients whom we have managed in the past. This difference might be explained by a relative deficiency of plasma and its constituents caused by the use of SAG-M blood. Our blood banks are aware of the problems that might be caused by massive transfusions of SAG-M cells and only issue it as a last resort. However, the packaging of SAG-M cells is very similar to that of packed cells and whole blood and so the heavily occupied anaesthetist may not observe when the change-over occurs. We feel that anaesthetists should be aware of the different properties of this blood product and recommend that additional plasma transfusion be given when this blood product it used during massive transfusion.

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Another example of Murphy's Law—mix up of pin index valves

Murphy's law,[1] whose exact origin is unknown, states that 'if anything can go wrong, it will'. The anaesthetic gas machine and the features intended to increase its safety sometimes provide evidence of the validity of this law.

The well-known pin index system was introduced to prevent the accidental fitting of a wrong gas cylinder to a yoke intended for another gas. This is ensured by having two pins projecting from the yoke. The cylinder of the correct gas has two holes corresponding to the two pins. The pin positions differ with different gases. We were recently presented with a cylinder of nitrous oxide (coloured blue) which could not be fitted to the nitrous oxide yoke. On closer inspection it was found that the cylinder had an oxygen pin index valve fixed on to it.

Steward and Sloan[2] described a helium cylinder with a nitrous oxide pin index valve, but we believe that this is the first occasion a mix up has been reported between two anaesthetic gas cylinders in everyday use.

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A policy for halothane?

Subsequent to the editorials in *Anaesthesia* and the *British Medical Journal* on the problems of halothane anaesthesia, our department issued the following guidelines for junior staff. 'Halothane will continue to be used. Halothane should not be used if the patient has had an anaesthetic with halothane within the previous 3 months, if it is impossible to find out what agents were used at that operation or if there is any history of liver dysfunction following an earlier anaesthetic.

We would be interested to know what policy other departments have adopted.

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Emphysema of the neck following epidural anaesthesia

We read with interest the letter from Dr S.M. Kilpatrick (*Anaesthesia* 1984; **39**: 499–500) outlining her hypothesis for the anatomical pathways of emphysema of the neck following lumbar epidural anaesthesia for obstetric delivery.

The first case of supraclavicular emphysema following obstetric lumbar epidural anaesthesia was reported in 1978.[2] We have had similar complications[3] in two elderly male patients following lumbar epidural anaesthesia for prostatectomy.

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Butterflies and guinea pigs

Learning how to put Butterfly needles into veins may be made easier by the following simple method (Fig. 1). The trainee sits and the plastic tubing of a previously unused Butterfly needle is made to simulate a vein by taping it with semitransparent tape (Micropore) to the trainee's thigh (theatre trousers or dress). The trainee then attempts to introduce the metal needle fully into the tubing.

Points which can be taught include the importance of keeping the vein (tubing) straight by maintaining slight tension on it with the thumb, the importance of the angle of approach, the feel of the different consistencies of skin (tape) and vein wall (tubing) and the importance of keeping the needle parallel with, and up the middle of, the vein (tubing) on its further introduction after entry, thus avoiding exit from the rear of the vein (or tubing) into the tissues (the trainee's leg). Different tapes can make the tubing more or less visible. The tubing lasts for at least a dozen attempts at puncture when these are made at slightly different points.

Twenty medical students or senior house officers have practised in this way. All have managed sooner or later to place the needle fully into the tubing and have thereafter achieved successful insertion in patients. Only one person so far has drawn (their own) blood.

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Care of the skin

Anaesthesia in the elderly patient requires special care for even the most simple procedures. One example is in the application of self-adhesive continuous monitoring electrocardiographic (ECG) electrodes. The skin of the elderly is fragile, especially when associated with chronic steroid therapy. 3M Red Dot with micropore backing, and Medicotest Silver/Silver Chloride pregelled ECG electrodes are used in this hospital with good effect. We have noticed that, however carefully the electrodes are removed, the underlying skin can be badly torn and this can add to postoperative discomfort.

A simple solution for such patients is to interpose a square of conductive gel pad between skin and the electrode adhesive surface. Littman 3M Defribrillator Pads are cut to size and are sufficiently adhesive and conductive to provide a good ECG signal and no skin damage at all.

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Anaesthesia, 1986, Volume 41, pages 1166–1170

Book reviews

Anaesthesia in the Elderly 1166
H.T. DAVENPORT
Acute Pain Management 1166
Edited by M.J. COUSINS AND G.D. PHILLIPS
Invasive Procedures in Critical Care (Clinics in Critical Care Medicine) 1167
Edited by C. L. SPRUNG AND A. GRENVIK
Guidelines in Clinical Anaesthesia 1167
P. HUTTON AND G. COOPER
Head Injury and the Anaesthetist 1168
Edited by W. FITCH AND J. BARKER
Cardiac Anaesthesia: Problems and Innovations 1168
S.DE LANGE, P.J. HENNIS AND D. KETTLER
Classical Anesthesia Files 1169
Edited by D.M. LITTLE JR.
Cardiovascular Actions of Anesthetics and Drugs used in Anesthesia 1170
Edited by B.M. ALTURA AND S. HALEVY
A Pocket-Book for Intensive Care 1170
J. TINKER AND S.M. JONES

Anaesthesia in the Elderly

H.T. DAVENPORT. Pp. 200, William Heinemann Medical Books Ltd, 1986. £10.95.

The substitution of 'elderly' for 'geriatric' hints at an empathy with the problems of old age. Throughout the early chapters Dr Davenport presents old age in its physiological and pharmacological contexts, showing that most deviations differ quantitatively only from the accepted for the healthy young adult who, probably erroneously in our ageing society, serves as the standard.

For most anaesthetists the keenest clinical challenge is encountered when pathological processes have caused severe distortion. In this book the author persuades us that the difficulties experienced with joint immobility, osteoporosis and covert cardiovascular and respiratory failure provide a potentially more rewarding clinical experience, especially when the problems have been predicted by a careful and knowledgeable pre-assessment.

Much of what Dr Davenport writes can equally apply to other age groups, hardly surprising when one remembers his previous paediatric writings. His is a practical message, resulting from years of practical clinical work. His attractively simple literary style and the clear and appropriate illustrations should not tempt the reader to believe that this is a simple message. Each section contains a wealth of detail and, for the indulgent, further relevant reading is provided by the plentiful end of chapter references, as well as a useful general bibliography.

This is an enjoyable and useful book, which should receive general acclaim. The limited index suggests to me that the author's intention is for this short work to be read from cover to cover, from which all anaesthetists would benefit.

F.R. ELLIS

Acute Pain Management

Edited by M.J. COUSINS AND G.D. PHILLIPS. Pp. 300, Churchill Livingstone, 1986. £29.95.

Albeit infrequently, it is indeed a pleasure when a book of exceptional quality is presented for review. In gathering together the offerings of an international group of contemporary experts in all aspects of the control of acute pain, Dr Cousins and Dr Phillips have produced such a volume. It is exemplary, not only on account of the contributions, but also because of the effective and yet sensitive editing which has resulted in few wasted words in the 300 pages, which are thus readable and piquant, as well as particularly instructive in basic scientific and clinical matters.

It is reassuring and heartening that the personal and psychological aspects of the pain and other discomforts suffered by patients are considered not only in the excellent chapter on psychological factors in acute pain management (Peck), but also in several of the others, however disparate their major themes.

The eleven chapters occupy 290 pages and cover the whole spectrum of problems associated with acute pain management from the development of pain management in critical care (Bryan-Brown) and neurological mechanisms of pain and the relationship of pain, anxiety and sleep (Phillips and Cousins) to therapeutic drug interactions (Nimmo *et al.*) and pain relief and modification of the stress response (Kehlet).

The final chapter is a somewhat novel group of clinically based homilies entitled 'Practical decision making', which gives sound guidance. It combines illustrations of clinical problems with the logical and commonsense route to produce optimal therapy. In this there is a noticeable lack of tunnel vision or dictatorial approach and consideration is shown for many facets of practice.

The high standard of textual content is matched both by the clear and well delineated print and the excellent diagrams and tables, which are masterly examples of clarity. The references at the end of each chapter are adequate, many are contemporary and give guidance to reading around each topic for those whose insatiable appetite for knowledge is matched only by their time to indulge this. Naturally, in dealing with such a contentious subject, there is room for criticism of some of the views expressed, but even having said this, one has to search diligently to find examples with which to quibble.

This is a book which every anaesthetist can afford to buy and cannot afford not to. It should be read and then read again and again, for it is not only full of valuable, easily assimilated information but, above all, it is readable. This is without doubt, a best buy for 1986 and, possibly, for many years to come.

K. BUDD

Invasive Procedures in Critical Care (Clinics in Critical Care Medicine)

Edited by C.L. SPRUNG AND A. GRENVIK. Pp. 294, Churchill Livingstone, 1985. £37.50.

The number of invasive and minor surgical procedures practised in intensive therapy units and high dependancy units seems to be ever increasing. In recent years, many 'How to do it' books have appeared on the market, with emphasis being placed on the technical skills required for each procedure and less upon their shortcomings. The contributors to this book have attempted a worthy objective, namely, to review the methods, indications, contraindications and complications of many of the invasive techniques which are practised in intensive therapy units and elsewhere. Some of the techniques described are practised only by specialists, but a knowledge of their potential value is useful.

The book opens with a chapter on intravenous and intra-arterial cannulation. Then, as might be expected from the predominant interest of one of the main authors, it continues with a very comprehensive review of the techniques of tracheal intubation (including tracheostomy). There are sections devoted to pulmonary artery catheterisation, chest drainage and pericardial aspiration. Other subjects covered include bronchoscopy and intestinal endoscopy, cardiac pacing, intra-aortic balloon pumping, intracranial pressure monitoring, haemodialysis and peritoneal dialysis. The extent of each section varies; in some it is a comprehensive review, whereas in others it is a practical description of how the procedure is carried out with minimal, although adequate, reference to the problems encountered.

The chapter on pulmonary artery catheterisation is very clear and well balanced. It starts with a list of the indications for using the technique. Emphasis is given to its shortcomings and hazards, most of which are well known, but often disregarded. The conclusion is that the indications for inserting such catheters should be restricted. The final paragraph of this chapter contains a thought-provoking sentence, namely, 'The use of this catheter has never been shown to improve the survival of critically ill patients'.

In some of the other sections there is some inevitable overlap; for example, successive chapters are devoted to chest aspiration and insertion of chest drainage tubes. The general standard of production is very high, although some of the illustrations are quite difficult to follow, particularly in the chapter on central venous cannulation and catherisation. The terminology throughout is in American English and, although most of the drugs used are familiar, it is conceivable that some readers may not recognise their names. The references are up to date and encourage further reading, the index is more than adequate and the price is reasonable. In summary, this book achieves what it has set out to do and can be recommended.

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Guidelines in Clinical Anaesthesia

P. HUTTON AND G. COOPER. Pp. 403, Blackwell Scientific Publications, 1985. £29.50.

'Anaesthesia, like every other branch of clinical medicine, is becoming more and more complex and specialized'. These words, taken from the foreword of this book, are intended to begin the explanation as to why it was written. Neither this statement nor the title of the book itself convey what is contained within. Basically, this work is a short textbook of medicine with short notes on how disease affects the anaesthetic regimen.

The preface explains that it is designed for anaesthetists in training in the United Kingdom, United States of America, Europe and Australasia. It does not contain descriptions of how to give anaesthesia. The text is in 12 chapters, arranged systematically: cardiovascular disease, the liver, renal disease and so on. Obstetric patients and children are two topics which are omitted from the book.

In each chapter, the pathological and pathophysiological background of disease are noted before general patient care, before, during and after surgery, are described. The principles of monitoring are considered in some depth, no doubt reflecting the interest of the authors. The extent to which each topic is considered varies greatly and the inconsistency must be a limitation of the work. It also makes it difficult to review, because one cannot generalise about the subject matter.

Practically no references are given within the text and I think this is an error. The authors state that they were surprised to find how frequently standard textbook recommendations depended upon relatively few anecdotal case reports. They have chosen to describe a logical approach and give a personal plan of action. In some ways this may be seen as an advantage to students, but it also makes its value more limited to others who might appreciate knowing the origin and supporting data for some of the statements made. The guide to further reading given at the end of each chapter is quite good and fairly comprehensive, but it would have been a simple matter to reference the text appropriately.

The book is well laid out, with a plan for each chapter, frequent headings and plentiful figures and tables. Specific problems to be anticipated in each disease are indicated by large dots. All of these, together with a reasonable index, make the book relatively easy to refer to for specific situations.

Thus, the book may meet its aim of being a short text of medical problems, to be consulted by trainees as they meet specific diseases. The limitations are the lack of consistency of coverage of topics, the absence of references and the frustration that the book falls between two stools: it is not quite a textbook of medicine and it is not really guidelines in clinical anaesthesia.

W.S. Nimmo

Head Injury and the Anaesthetist

Edited by W. Fitch and J. Barker. Pp. 290, Elsevier Biomedical Press, 1985. US $81.50.

When junior anaesthetists ask what to read concerning the anaesthetic management of head injuries, I invariably used to recommend selected chapters in a book *Management of Head Injuries* by Bryan Jennett and Graham Teasdale of the University of Glasgow, which gives an excellent account of the pathophysiology, assessment and practical management of head injury. Now having read the following book, I am inclined to change my mind. *Head Injury and the Anaesthetist*, edited by William Fitch and John Barker has contributions largely but not exclusively drawn from Glasgow and, as its title implies, is specifically tailored for the anaesthetist. It is Volume 14 of the series Monographs in Anaesthesiology.

The first two chapters give a very clear account of the pathology and pathophysiology of head injury and incorporate data derived from studies by the authors themselves, which gives the reviews a certain authority. Sheila Jennett then considers the pulmonary and neurogenic causes of hypoxaemia in head injury, followed by Graham Teasdale who describes the use of the Glasgow Coma Scale in the clinical assessment of head injury. Next follows a very important chapter on the immediate care and transportation of the head injured patient. John Barker then gives an interesting account of various anaesthetic agents which could be used in anaesthesia for head injury. In the preface, the editors state that anyone looking for a recipe on how to treat the head injured patient will be disappointed and I was somewhat disappointed that no indication was given of how anaesthesia for head injury was managed in Glasgow. Many readers will look for such information and guidance. Jean Horton does give good practical advice in her chapter on the postoperative care of the head injured patient.

The book is dedicated to the memory of Professor Gordon McDowall and includes a chapter by him on artificial ventilation in the management of the head injured patient, which is a model of clarity and balanced argument. There follow informative chapters on intracranial pressure monitoring, the management of facial and chest injuries and a very worthwhile American contribution on the use of barbiturate therapy. The final two chapters cover brain death and future developments in the care of the head injured patient.

Each chapter is a review of a topic by an expert in the field and an excellent source of references. The book will be of interest to all anaesthetists, since we all deal with head injuries from time to time, and it should find a useful place in all anaesthetic libraries. Some of the photographs I found to be rather dark and dated, but the book is otherwise well printed in hardback on good quality paper.

L. Loh

Cardiac Anaesthesia: Problems and Innovations

Edited by S. de Lange, P.J. Hennis and D. Kettler. Pp. 200, Martinus Nijhoff, 1986. £33.25.

This book, despite its title, is the proceedings of a symposium entitled *Recent Advances in Cardiac Anaesthesia*, which was held in Leiden in the Netherlands in May, 1985. Primarily from this meeting came the seed which germinated to form the European Association of Cardiothoracic Anaesthesiologists in June this year. This volume contains 21 papers, which range from a few short case reports, through some descriptions of monitoring and measurement techniques, to some clinical anaesthesia and perfusion papers. This reviewer did not consider that the book lived up to its title as far as problems and innovations were concerned. However, some of the papers included should provoke discussion and interest in the target audience which, one presumes, is practising cardiac anaesthetists. In some places the translation from the original papers into English makes reading a little difficult.

Some of the contributions have titles which suggest that the paper will cover an area which is a recognised problem in cardiac anaesthesia, but frequently this is not the case. The section headed 'The use of invasive monitoring techniques in cardiac surgery' addresses itself solely to pulmonary artery catheters and contains the view that a pulmonary artery catheter is valuable in every cardiac patient coming to theatre. The only discussion seems to be about at what stage of the procedure it should be inserted.

The paper on profound hypothermia and circulatory arrest does describe some new and interesting work; the work on sequential myocardial depressant and non-depressant anaesthesia may also stimulate thought. One of the few papers which does describe a real innovation is devoted to transoesophageal 2-D echocardiography and this may stimulate the reader to consider the diagnostic possibilities for this technique in his own unit.

Unfortunately, this book is not well presented. The contents page is difficult to read and quite difficult to find. Each paper appears with a different type face, different margins and different line spacing. In one or two papers the print is so close and the line spacing so small as to render reading a physical effort. Frequent abbreviations appear without definition. Many of the illustrations and figures have been poorly reproduced; some of them are so small that the legends are readable only to the myopic, while others appear with no interpretation or discussion at all. Unfortunate spelling and typographical errors occur rather more frequently than editors of medical journals would normally allow: on one randomly selected page I found four separate errors. The index is clear and easy to use, but probably superfluous.

This particular form of direct reproduction of the contributors scripts may reduce costs in the production of a book, but at a price of £33.25 one anticipates that many contributors will be disappointed in the way that their work has been presented.

J.D. Kneeshaw

Classical Anesthesia Files

Edited by D.M. Little Jr. Pp. 335, Wood Library–Museum of Anesthesiology, 1985. $32.00.

Each edition of the American journal *Survey of Anesthesiology* between 1957 and 1981 published a Classical File. This consisted of the full reprinting of a fundamentally important paper related to anaesthesia. The topics selected usually dealt with historically important events from the recent or distant past of anaesthesia, or with seminal contributions to the clinical practice or the basic sciences of the specialty. To each reprinting was added a brief supporting essay, which outlined the importance and relevance of the particular article.

For the whole of the 25 years between 1957 and 1981, each article was selected by one distinguished New England anaesthetist, the late Dr David M. Little, Jr, who also wrote all the accompanying essays. These added a sense of historical perspective, and, being refreshingly argued and cogently reasoned, were erudite, instructive and entertaining. His selection was masterful and covered journals from many different countries and many different ages. They ranged, for example, from the report of blood transfusion in 1666 to the dissertations of 1961 by Linus Pauling on the molecular theory of general anaesthesia and by Jude, Kouwenhoven and Knickerbocker on external cardiac massage. By the time of his death in 1981, Dr Little had, in this format, republished and commented upon most of the classic contributions on which the practice of anaesthesia was at that time based.

This unique series of 150 classical files was, by and large, overlooked by many potentially interested anaesthetists, especially in Britain, and it is therefore a pleasure to record the reprinting of David Little's work in one single volume. This has been collated and published by the Wood Library–Museum of the American Society of Anesthesiologists, which body deserves our congratulations on their project.

There are however, features of this volume which make it less than perfect. Its layout is somewhat confusing and it is not easy to find one's way about the text without consulting both the contents and the index in turn; the index itself seems incomplete. Unfortunately, for considerations of space, the editors have been compelled to omit the classical articles themselves, and have in their stead reproduced far too brief, and frequently uninformative summaries. One might have hoped that space could have been found for more of the original articles (perhaps, where appropriate, the discussion section). Similarly, Dr Little included, in his original columns, both an article's illustrations and list of references, but again for reasons of economy these are not included in the book form. On the other hand, Dr Little's own essays are reprinted in full and it is the perusal of these which makes this volume so attractive and worthwhile. (It is a pity that Dr Little, who was wont to make some intriguing and provocative *ex cathedra* statements, did not add lists of references to his own essays in support of these remarks.)

These criticisms diminish the value of this reprinted work as a complete historical text and compilation of source material, although the original editions of the *Survey of Anesthesiology* are still to be found in various libraries. Nonetheless, the volume is a delight to read and should appeal to anyone with an interest in the evolution of our specialty.

R.H. Ellis

Cardiovascular Actions of Anesthetics and Drugs used in Anesthesia

Edited by B.M. Altura and S. Halevy. Pp. 268. Karger, 1986. £76.50.

This is a small print book, not in the optical sense, but in the sense used by examiners to describe the knowledge of a candidate who knows obscure facts that the examiner does not, but who fails to mention the obvious. It is Volume 1 of what is advertised as a two-volume work (the second being on regional blood flow and clinical considerations). If the price quoted above is for this first volume alone, it costs three to four times as much as a British produced book of comparable size.

There are nine chapters, seven from USA centres, one from France and one from Germany; each addresses exclusively the cardiovascular effects of drugs which are given in the main for purposes other than having an effect on the cardiovascular system. Thus, there are chapters on general anesthetics, (the spelling is American throughout), intravenous anesthetics, narcotic analgesics, neuroleptics, relaxants, and local anesthetics and two others on neurohumoral substances and interactions between anesthetic and cardiovascular medications. Some chapters are extensively referenced (over a hundred references for thirty small pages of text), while others are relatively sparse. Applying a moderately severe test for up-to-dateness, roughly 13% of the reference date from 1982 or later.

The chapters generally make turgid reading; an honourable exception is that by Sonntag and Larsen from Göttingen, prompting the thought that if two German authors can write good English, why can't the Americans? The chapter on intravenous anesthetics suffers from the inclusion of drugs which have largely disappeared (Althesin, propanidid) or are little used (ketamine, methohexital), but says too little about ones which have been actively investigated recently (etomidate, propofol). The chapter on neuroleptics by Deligné (translated by Deslauriers) will fascinate the British reader for the glimpse of fundamental differences in practice between France and Britain. Who amongst us could write two sentences, let alone two pages each, on the circulatory effects during anesthesia of levopromazine, perimetazine, thioxanthene and chloroprothixene?

Frankly, I find it difficult to visualise the readership for this book; far too little data is available in man and often that has been obtained in somewhat artificially restricted conditions. The expert investigator knows it and will be more up-to-date than any book can be. Many of the effects recounted are relatively minor, perhaps no more extreme than are those associated with falling asleep or taking modest exercise. The average anaesthetist knows about them, but discounts them for practical purposes.

Anyone with a high respect for the English language should be warned that it is particularly unsuitable for them. One author tells us that 'the rapid advance in the research laboratory ... has resulted *literally* (my italics) in an explosion of information'. Some authors give us boring or ill-constructed sentences. Fortunately, most of them appear to be able at least to write ately, most of them appear to be able at least to write better than the editors whose Preface actually starts with a sentence which uses a singular subject and a plural verb. Let us hope for better things from Volume two.

M.D.A. Vickers

A Pocket-Book for Intensive Care

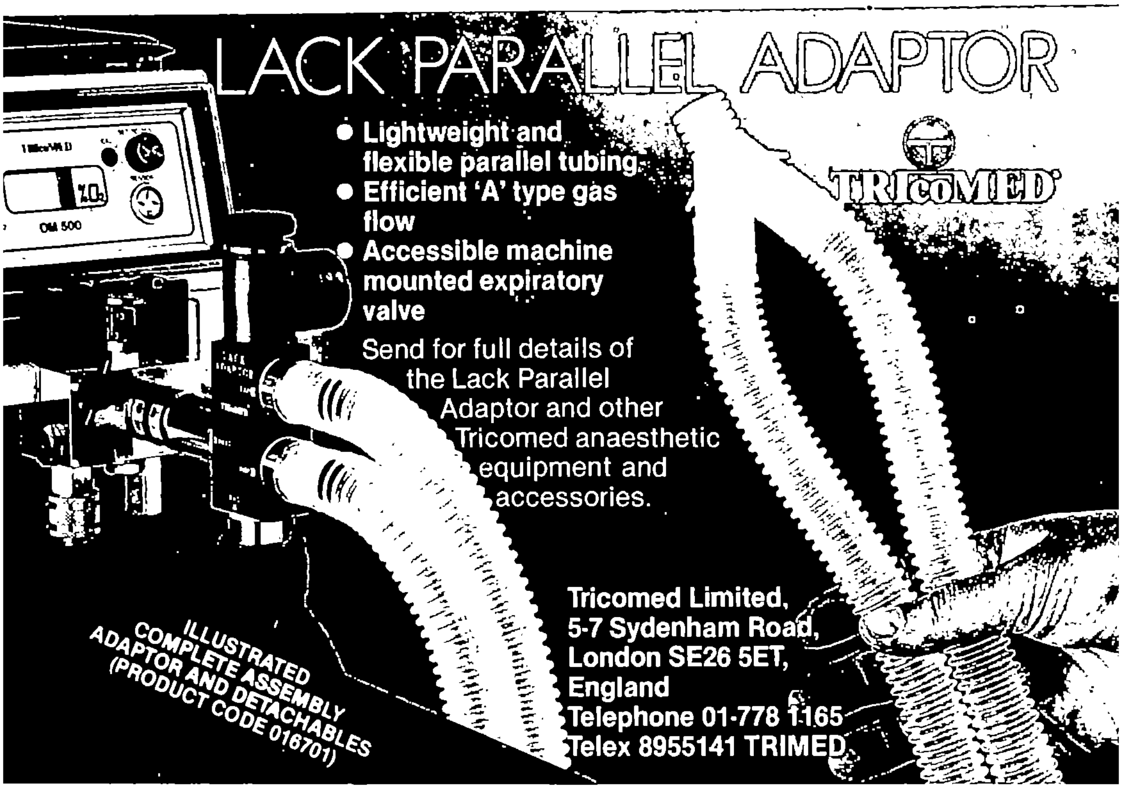
J. Tinker and S.M. Jones. Pp. 150, Edward Arnold, 1986. £7.25.

The authors of this little book have compiled it as a source of useful, practical information for medical and nursing staff working in intensive care units. They have been successful. It contains, system by system, physiological and technical data, drugs and their doses and practical techniques. It is a mine of information which fits easily into a white coat pocket and I have used it frequently. It is particularly useful for reference about drug doses. The section on toxicology is very valuable, giving the normal plasma concentrations, concentrations associated with severe toxicity and specific forms of management.

There are, however, some serious omissions. There is nothing on opioid drugs for the control of patients on mechanical ventilation of the lungs or on pain relief. Automatic ventilation must be the commonest intensive care procedure, but it is not mentioned. The equipment list for tracheal intubation does not include a bag and facemask. There is no guidance on how to prevent the aspiration of gastrointestinal contents during this procedure.

It is to be hoped that these details will be remedied in the next edition. I shall then not only buy one for the unit, but make sure that there is one by every bed.

J.F. Searle



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Index of computer programs

026.1.13

Author J.A. Thompson (Hinchingbrooke Hospital, Hinchingbrooke Park, Huntingdon, Cambridge PE18 8NT).

Title Theatre List Statistics.

Description This program is designed to calculate, display and print out statistics on routine operating lists. These statistics include theatre utilisation %, list time used, list overrun, list underrun, numbers and reason for cancellations, number of cases (major, intermediate and minor). The program meets the Korner report requirements for theatre operating list statistics. It includes a graphical display and print-out of list sessions, as well as a monthly/weekly summary of list activity.

Language BBC Basic.

Computing facility BBC with compatible printer and double disk drive. The BBC needs to have a StardataBase ROM installed.

027.1.42

Author C. Nixon (Department of Anaesthesia, University College Hospital, Gower Street, London, WC1E 6AU).

Title Fluid and Nutrition Program for Paediatric Intensive Care

Description This program was designed for use in paediatric intensive care units to calculate the fluid, electrolyte and calorie intake along with nitrogen, electrolyte and water balance. It is not designed to suggest fluid and nutrition therapy, but merely to calculate what the patient has received. The program allows the user to enter crystalloid intake in terms of dextrose, saline, potassium and calcium, and nutritional solutions from a selection of five standard solutions, with the option of a 'special solution' according to requirements. Enteral feeding solutions may be selected from a list of available solutions and concentrations. A results page gives the sodium, potassium, calcium, magnesium, phosphorus, protein, carbohydrate, fat, water and calorie intake, as well as indicating the intravenous glucose load (mg/kg/minute) and the percentage of calories derived from protein. The program is easy to use and allows any section of the program to be accessed in any order to allow correction or alteration. For calculation of nitrogen balance, the program prompts the user to enter urine output (ml/day) proteinuria (g/dl), urinary urea nitrogen (mmol/litre) and change in blood urea (mmol/litre/day). Assumptions have been made for obligatory nitrogen loss from skin and stool.

The user is guided through the program by menus which appear at the lower border of the screen. Pressing the appropriate function key selects from the chosen menu option. The program can be tailored to individual requirements and standard hospital solutions can be substituted if desired; it would also be suitable for use in adult intensive care with some modification.

Language Microsoft Basic

Computing facility Digital PDP-11 minicomputer with Hewlett Packard HP2023A terminal.

028.1.12

Author P. Hommelgaard (Department of Anaesthesia, Silkeborg Hospital, DK8600 Silkeborg, Denmark).

Title Computing Questionnaire

Description The program produces a questionnaire with more than 30 variables, each with up to 20 codes. It places the data in one or two dimensional tables and calculates simple statistics (percent, mean, SEM, variance, Chi square). A search can be

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Details of programs to be included in this catalogue should be sent to Dr M.J. Harrison, Department of Anaesthesia, Nottingham City Hospital, Hucknall Road, Nottingham, NG5 1PB. They should be of relevance to anaesthesia or intensive care. Programs that involve the application of the basic sciences, or teaching, will also be accepted. Further details of the programs can be obtained from the department or person directly involved.

made through all the data or up to five variables with specified codes can be used as the search criteria. The total program consists of five parts: library, data input, data change, one dimensional table, two dimensional table and statistics.

If an investigation can be represented in coded variables, several thousand patients could be handled by the program.

Language MS-Basic (MS-DOS 2.0 or higher)

Computing facility Apricot PC with disk drive and printer.

020.2.13

Author C.J. Hull (Department of Anaesthe Victoria Infirmary, Newcastle upon T 4LP).

Title Shortlist.

Description Automates the task of coll ranked preferences of up to 22 selection c members from up to 60 candidates, t ranked shortlist. Simple, conversational with extensive error-trapping; easily r secretary.

Language HP Basic, Microsoft Basic

Computing facility Hewlett-Packard 85, Apricot. Sirius. Listing is available on r send an initialised disk.

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Anaesthetic literature

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Anaesthesia, 1986, Volume 41, page 1180

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Pre-assembled components have become misshapen or assemblies have fallen apart and do not make a satisfactory joint when reassembled. Individual components may distort if placed under other items. Both these effects have followed autoclaving and users are recommended to process plastic conical fittings, which are claimed to be re-usable, only in accordance with the manufacturers' recommendations. Single-use items should not be re-sterilised or reused.

Erratum

Anaesthesia, 1986, Volume 41, pages 703–707

Nitrous oxide anaesthesia and vomiting

D. S. LONIE AND N. J. N. HARPER

The sentence beginning on line 17 of the Patients and methods section (p. 703) should read: In group A, anaesthesia was maintained with nitrous oxide 67 percent in oxygen and 1.25 minimum alveolar concentration (MAC)...

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The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

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BOOKS AND OTHER MONOGRAPHS

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OSLER AG. *Complement: mechanisms and functions.* New York: Prentice-Hall, 1976.

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American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences.* 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

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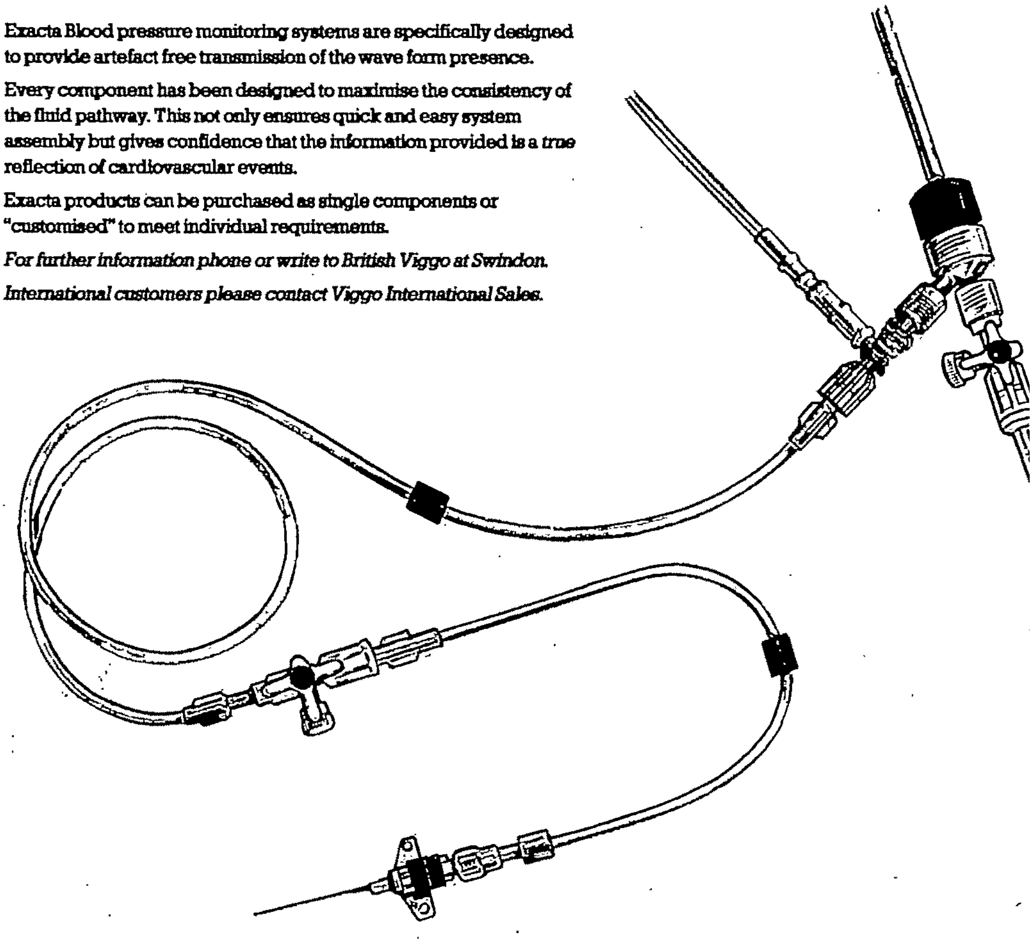

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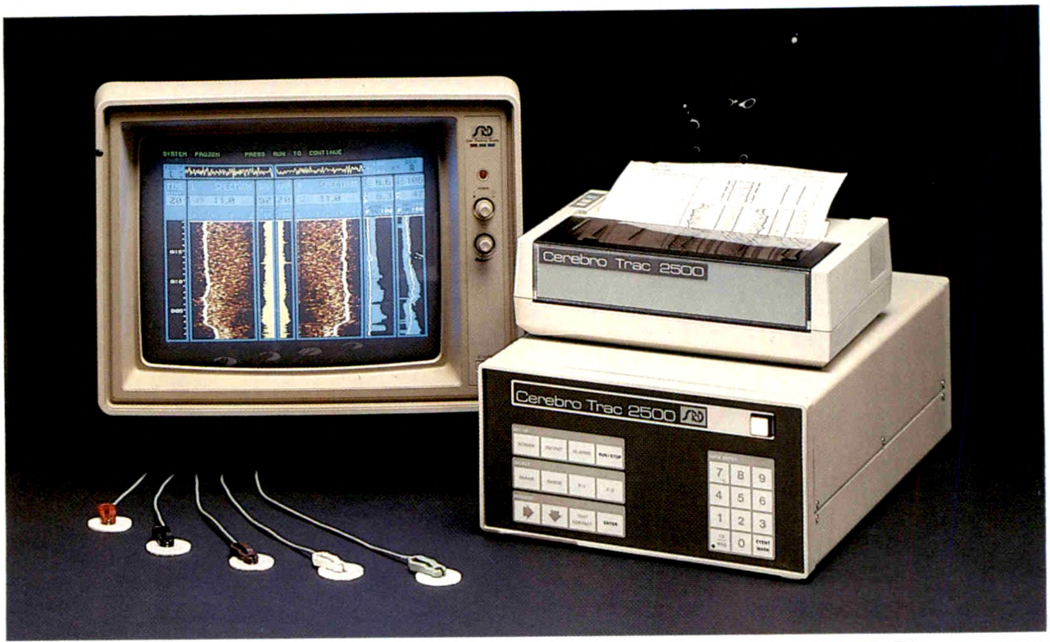

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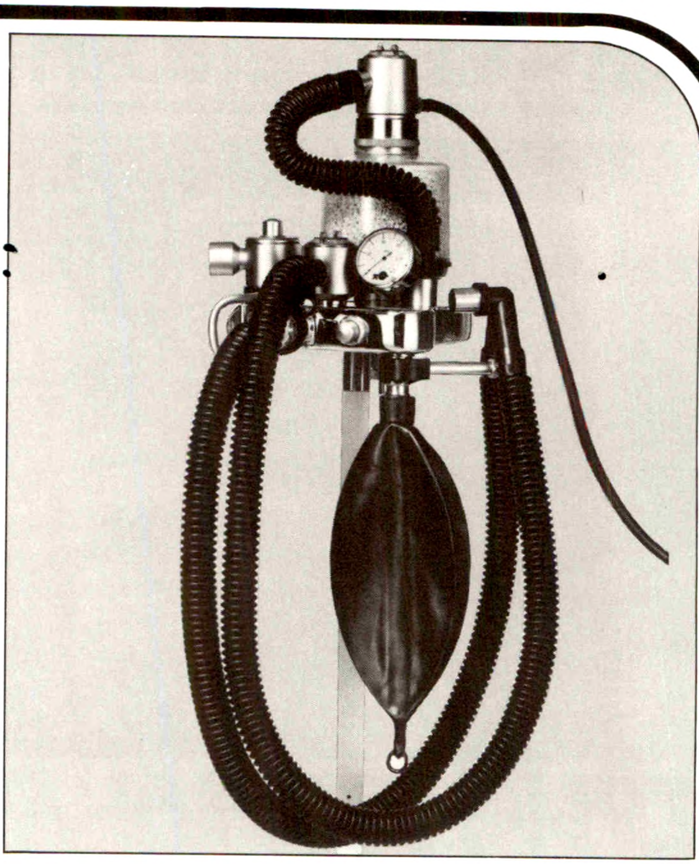

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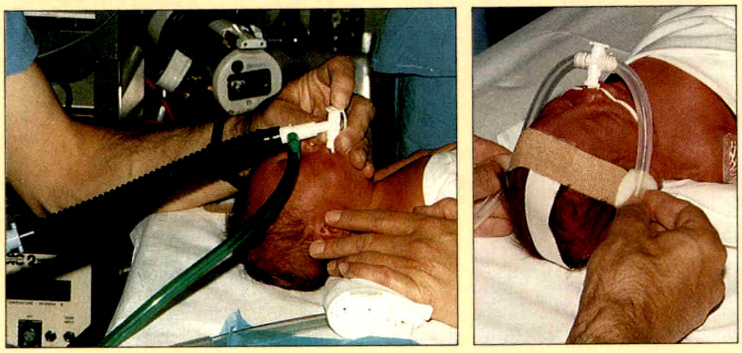

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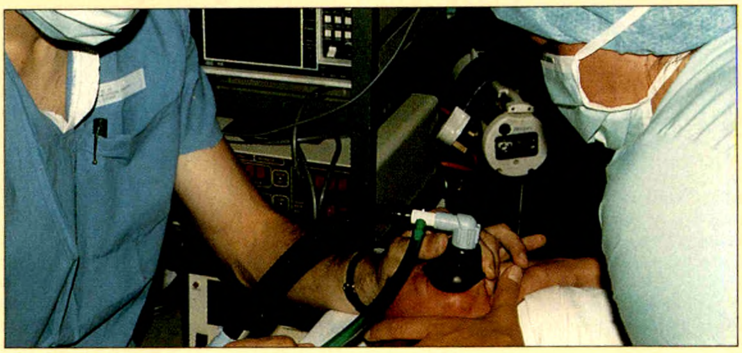

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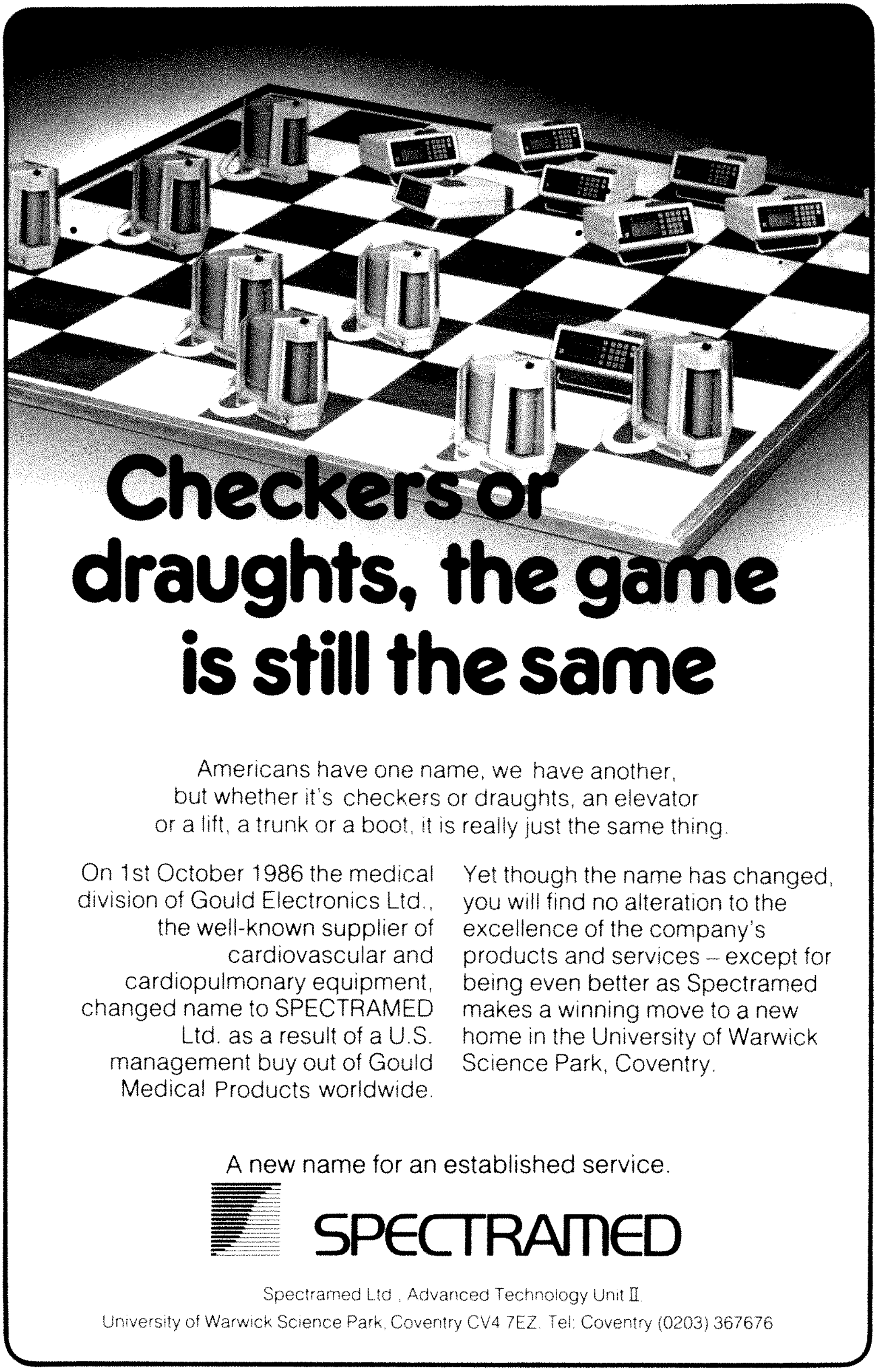

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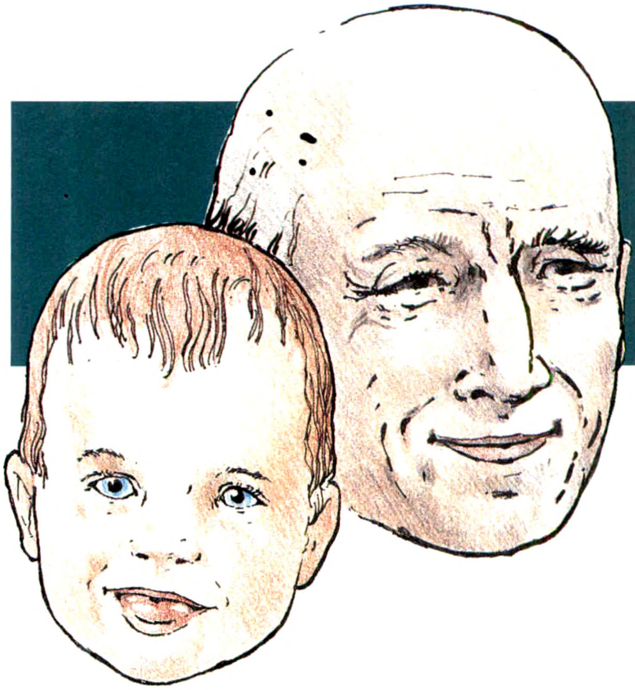

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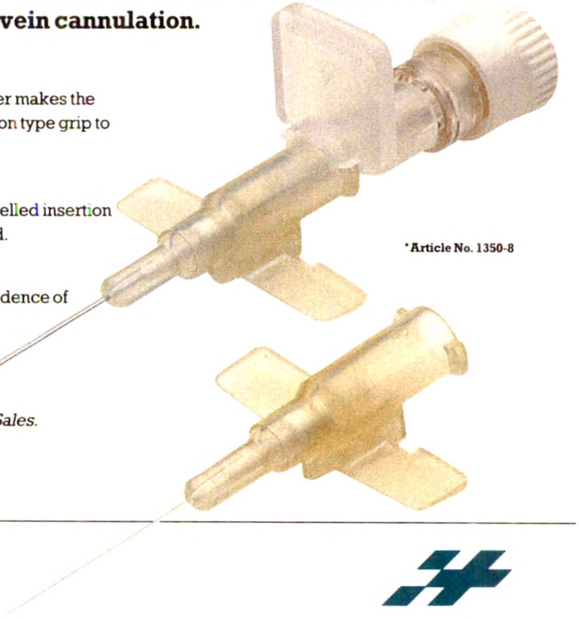

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Anaesthesia, 1986, Volume 41, pages 1181–1183

Editorial

A career post—with intensive therapy?

Several attempts have been made over the years to define the qualities and qualifications expected of the doctor whose responsibilities include involvement with an intensive therapy unit (ITU). With a few outstanding exceptions, in the United Kingdom such responsibilities originally rested with anaesthetists who gave freely of their skills, interest and time without sessional recognition. Gradually, and belatedly, but with increasing frequency, many now have some sessional allocation for these duties.

The monolithic structure of the National Health Service has created difficulties for any doctor who wishes to do something which is not historically identified as being within his specialty. In other parts of the world this rigidity is not seen and there may be more than one route to recognised specialist status. This has sometimes led to wasteful duplication of training programmes, to professional conflict and to the confusion of the public at large.

In the United States of America, intensivism is well established and it was hoped that a general agreement would lead to the recognition of one system of board certification for doctors of any specialty who wished to practise intensive therapy.[1] However, the agreement was short-lived and there are now five distinct specialty boards (anaesthesia, internal medicine, paediatrics, surgery and neurosurgery), each of which give certification after a period of approved training.[2] There is another specialty board for emergency medicine which may overlap with these. The clinical scope of those with board certification is very limited and it is usual to find three or more ITUs of different types with separate staffing structures in quite small hospitals.

In Australasia, medical graduates who have obtained the primary fellowship in anaesthesia can then elect to take the Fellowship of the Faculty of Anaesthetists (Int. Care) of the Royal Australasian College of Surgeons. The Royal Australasian College of Physicians has established a separate system of training for physicians who wish to practise in an ITU.[3] This ambiguity has led to professional ill-feeling, but both systems are recognised by the Federal Government.

There is no standardised system in Europe, but in most countries anaesthetists play a greater or lesser part in ITUs. The range of responsibilities is wide; for example, in France, in one hospital, the anaesthetists may be responsible for both the ITU and the accident and emergency services whereas in another hospital nearby, they may play a subsidiary role in both.

For a variety of good reasons, the Department of Health of the United Kingdom appears to be in no hurry to recognise a specialty of intensivism. Recently, a committee composed of representatives of the Faculty of Anaesthetists and Royal Colleges of Physicians and Surgeons (the Interfaculty Liaison Committee) published guidelines for the training of doctors who wish to spend a significant part of their weekly work in an ITU.[4] The guidelines are intended for the assistance of trainees in medicine, surgery and anaesthesia. In summary, they recommend that there should be cross-fertilisation between specialties, such that the physician or surgeon should spend time in anaesthesia while the surgeon or anaesthetist should spend time in selected medical posts. In addition, all trainees would have a 2-year apprenticeship in one or more ITUs approved for that purpose by the committee. It is intended to establish pilot schemes of this type in the Northern and South Western regions of the National Health Service. The Royal College of Physicians has promulgated similar guidelines in its training handbook.[5]

The recommendations for the length of time spent in each specialty are uneven, but the overall idea is, on the face of it, unexceptionable. The liaison committee has not yet given its views on some of the most intractable problems. The first of these is that there are not nearly enough 'medical' training posts for all those candidates, in addition to the intending physicians, whose general professional

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training (GPT) requires such experience. Those competing for such posts now include trainees for the Membership of the Royal College of General Practitioners and the Fellowship of the Faculty of Radiologists. In spite of this difficulty, many trainees in anaesthesia who hope to work in an ITU have undergone such training and a number have acquired the Membership of the Royal College of Physicians before completing their GPT in anaesthesia. What category of trainee do such people become? Are they physicians with the anaesthetic fellowship or *vice versa?*

Much the most important problem concerns the allocation of consultant posts and the job description. At present, almost the only posts which are advertised which carry intensive therapy sessions are in anaesthesia although it is recognised that some other consultants, for example, those in cardiothoracic and paediatric surgery, and some paediatricians, will spend some time in the recovery room and specialised ITU. It is relatively easy for the anaesthetist who has double qualifications because if a suitable consultancy in anaesthesia with intensive therapy sessions does not materialise when he is ready for it, he can become a 'straight' anaesthetist and await events. By the same token, after a number of years, the ITU anaesthetist may feel the need to reduce his ITU commitment and he would then have little difficulty in assuming more anaesthetic sessions. However, if a 'medical' or 'surgical' trainee follows the course of instruction recommended by the Joint Liaison Committee he will spend an extra 2 or 3 years in training, after obtaining the MRCP or FRCS diploma, outside his first choice specialty within medicine or surgery. Inevitably, he will not have had time to establish himself as a surgeon or as a physician during this period, particularly since the days of the generalist are almost over. Consequently, if no suitable consultant post materialises, he may well join the ranks of the time-expired senior registrars.

If the Department of Health is now willing to assume the responsibility for such career posts with intensive therapy as a subspecialty there could be awesome practical difficulties. The posts would probably have to be distributed proportionally, as, for example, to include ITU sessions in one in every four anaesthetic, one in every eight medical, and one in every twelve surgical, consultant posts. Retirement vacancies could create even greater difficulties than at present, with members of the three relevant specialties disagreeing as to which one should assume the vacant sessions.

In addition to the shortage of medical training posts referred to above, there would be a need for additional anaesthetic registrars to allow for the cross-fertilisation of specialties. The anaesthetic and surgical registrar could probably accept the transition to medicine without much difficulty. However, the practical responsibilities of the anaesthetic registrar could not be taken on by the others without further training and delay. The alternative would be to make all such posts supernumerary, but this would inevitably reduce 'hands on' experience for all three groups of trainees.

To the writer, it appears that the problems engendered by this suggested training programme are greater than the relatively small one they are intended to resolve, namely, the recognition that intensive therapy and anaesthesia go naturally together. The diploma of Fellow of the Faculty of Anaesthetists of the Royal College of Surgeons is designed to contain a significant proportion of ITU-related topics. Large numbers of anaesthetic trainees have augmented this by voluntarily spending extra time in suitable medical posts, with or without taking the MRCP.

One of the most important aspects of intensive therapy is the recognition of the need for cross-consultation. The anaesthetist is, of necessity, at the centre of cross currents of consultation throughout his professional life. This fact, together with his training and practical skills, fit him for the role in the intensive therapy unit which should now be recognised rather than taken for granted.

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J.C. STODDART

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Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; **1:** 532–5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Index to Volume 41 (1986)

Would subcribers kindly note that the Index for Vol. 41 (1986) will appear separately in the January issue, Vol. 42 No. 1.

News and Notices sections

The first issue of each quarter will contain full News and Notices sections.

Copy dates for these will be: 12 December 1986 for April 1987, 13 March 1987 for July 1987 and 12 June 1987 for September 1987.

Supplementary News and Notices sections will be published in other issues but they will contain only material which requires publication before the next full News and Notices section.

Anaesthesia, 1986, Volume 41, pages 1184–1188

Benzodiazepine antagonist Ro 15-1788

Antagonism of diazepam sedation in outpatients undergoing gastroscopy

L. KIRKEGAARD, L. KNUDSEN, S. JENSEN AND A. KRUSE

Summary

In a double-blind, randomised trial the efficacy and safety of Ro 15-1788, a new benzodiazepine antagonist, was assessed in forty adults undergoing gastroscopy under diazepam sedation. Criteria of efficacy were the degree of sedation and anterograde amnesia. There was a significantly faster recovery of the patients after the injection of 0.6–1.0 mg of Ro 15-1788 than after placebo. Patients were awake shortly after Ro 15-1788, but remained drowsy or asleep after placebo administration. There were no side effects of note.

Key words

Hypnotics, benzodiazepines; diazepam.
Antagonists, benzodiazepines; Ro 15-1788.

Benzodiazepines are often used as sedatives in connexion with minor diagnostic procedures such as gastroscopy. The duration of action of these drugs depends on the chemical structure, administered dose, type and condition of the patients and various other factors such as concomitant medication. However, in many clinical situations the central effects induced by the administration of benzodiazepines are of longer duration than necessary. The recently discovered benzodiazepine antagonist Ro 15-1788, allows the reversal of the central depressant effects of benzodiazepines. This would have the advantage of speeding the recovery from sedation, thereby shortening the monitoring period and improving patient collaboration.[1–4]

The aim of this study was to evaluate the efficacy of Ro 15-1788 in reversing the central effects of diazepam when administered to outpatients undergoing gastroscopy, and also to evaluate the safety (local and general) of Ro 15-1788.

Methods

Forty consecutive patients of both sexes of ASA grades 1 and 2, aged 18–70 years, undergoing gastroscopy at the Aarhus Kommunehospital, were studied in a double-blind, randomised trial. The study was carried out in accordance with the Helsinki II Declaration and approved by the ethics committee of the county of Aarhus. Informed consent was obtained. Patients who were receiving other centrally acting drugs, had neurological disease or who were pregnant were not studied.

Premedication consisted of intramuscular atropine 0.01 mg/kg half an hour before gastroscopy. A catheter was placed in a vein in the back of both hands. Lignocaine spray was applied to the pharynx. After the injection of diazepam, in the form of diazemuls, 0.3–0.5 mg/kg intravenously in the right hand, the gastroscopy was performed.

On completion of the diagnostic procedure 0.2

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Table 1. Demographic data. Median (range)

Group	*n*	Male/female	Age (years)	Weight (kg)	Height (cm)
Ro 15-1788	20	10/10	57 (24–70)	64.5 (42–90)	168 (153–183)
Placebo	20	11/9	46 (19–70)	68.0 (43–86)	169 (156–187)

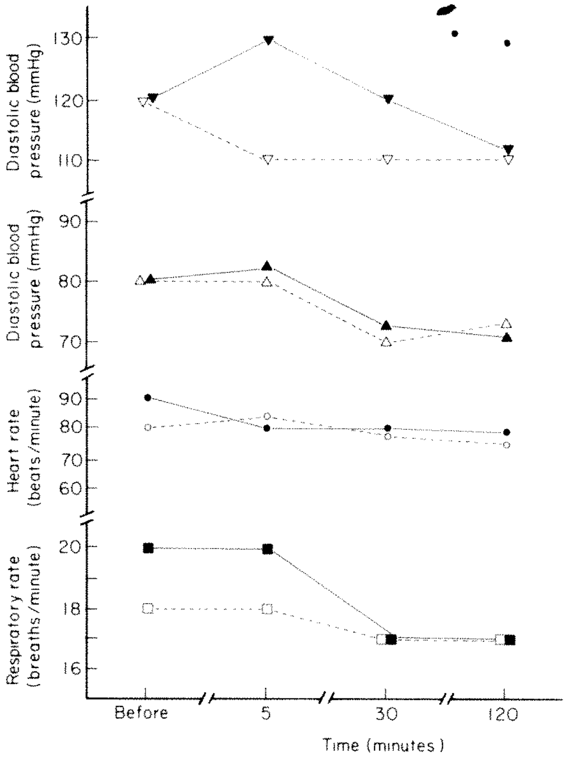

Fig. 1. Effect on the cardiopulmonary variables. Filled symbols, Ro 15-1788; empty symbols, placebo.

mg of Ro 15-1788 or the placebo equivalent (vehicle only), was injected in the left hand followed by additional doses of 0.2 mg every minute until the full effect was achieved (i.e. complete reversal of sedation), or up to a maximum of 1.0 mg. Before injection of Ro 15-1788 or placebo, and 5, 30 and 120 minutes after injection the following variables were noted: blood pressure, heart rate and respiratory rate.

The degree of sedation at these times was assessed on a five-point scale as follows: 1, fully awake; 2, awake but not alert; 3, drowsy; 4, sleeping but rousable; 5, sleeping but not rousable. The amnesia was recorded at 120 minutes by asking the patients: 'did you remember anything about the gastroscopy?' and 'did you remember being in the operating theatre after the gastroscopy?'

Central side effects were recorded after 5, 30 and 120 minutes. Arterial blood gases were measured 15 minutes after injection of Ro 15-1788 or placebo. Local side effects in the form of redness or pain at the injection site of Ro 15-1788 or placebo were recorded at 5 and 120 minutes.

Results are given as median and range. Comparability between groups was assessed by Mann–Whitney and Fisher's exact tests. The data in Figs 1 and 2 were analysed by a combination of Mann–Whitney and Friedmann tests corresponding to analysis of variance for a two factor design (drugs and time).

Results

There were 20 patients in each group; these were comparable with regard to sex, age, weight,

Table 2. Trial drug dosages and gastroscopy time. Median (range)

Group	n	Dosage of diazepam (mg/kg)	Gastroscopy time (minutes)	Dosage of Ro 15-1788/ placebo (mg)
Ro 15-1788	20	0.40 (0.30–0.70)	15.5 (5–40)	1.0 (0.6–1.0)
Placebo	20	0.41 (0.30–0.81)	18.5 (10–37)	1.0 (0.6–1.0)

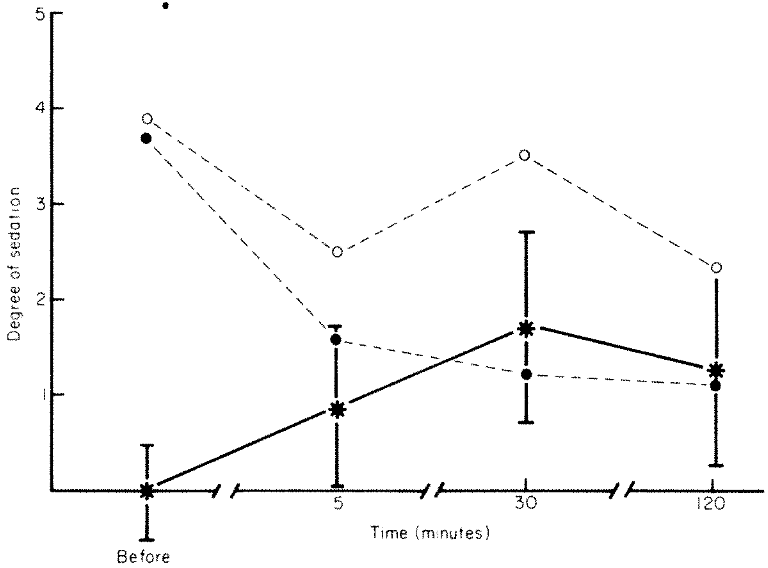

Fig. 2. Degree of sedation. ●, Ro 15-1788; ○, placebo; *Median difference with 95% confidence limits; 1, patient awake, and alert; 2, patient awake, not alert; 3, patient drowsy; 4, patient sleepy, arousable; 5, patient sleepy, not arousable.

height (Table 1), dosages of diazepam, Ro 15-1788 or placebo, gastroscopy time, heart rate, blood pressure and respiratory rate before treatment (Tables 1 and 2, Fig. 1). There was no intergroup difference with regard to heart rate and blood pressure (Fig. 1). There was a significantly higher respiratory rate in the treatment group and a significant fall in respiratory rate with time (Fig. 1).

There were no between group differences in the $Pa\text{O}_2$ or $Pa\text{CO}_2$ (Table 3). Ro 15-1788 markedly reduced the degree of sedation (Fig. 2); the difference from placebo was statistically significant ($p<0.05$). Five minutes after administration of the benzodiazepine antagonist the patients were awake and remained so during the whole observation period. In the placebo group, most patients remained drowsy and their degree of sedation deepened again at 30 minutes after trial drug administration.

The amnesia induced by diazepam was eliminated in 85% of the treated patients against 35% in the control group ($p<0.01$) (Table 4). Three patients in the treatment group and one in the control group were slightly confused immediately after the reversal of the sedation. One patient in the treatment group suffered from headache. There were no other side effects.

The only sign of local intolerance was a short-lasting redness at the injection site 5 minutes after injection in one patient who received Ro 15-1788.

Discussion

Benzodiazepines (BZ) enhance transmission at the GABA-ergic synapses in the central nervous system (CNS), modifying the GABA receptor–chloride channel coupling. The main effect of this process is inhibitory and, when enhanced, it

Table 3. Arterial blood gas analyses. Median (range)

Group	*n*	Pa_{O_2} (kPa)	Pa_{CO_2} (kPa)
Ro 15-1788	20	9.6 (7.7–12.7)	5.5 (4.7–6.5)
Placebo	20	10.2 (7.2–12.9)	5.2 (4.3–6.2)

Table 4. Anterograde amnesia, judged at 120 minutes post administration

	Ro 15-1788 yes/no	Placebo yes/no
Do you remember anything from the gastroscopy?	2/18 (90%)	4/16 (80%)
Do you remember being in the operating room after the gastroscopy?	17/3 (15%)	7/13 (65%)

exerts anxiolytic, sedative, anticonvulsive and hypnotic effects.[3–4]

The imidazobenzodiazepine Ro 15-1788 has a high affinity for the benzodiazepine receptor and therefore competes with other benzodiazepines for the same binding sites. In theory, in the absence of a detectable intrinsic effect,[4] it functions as an antagonist to the central effects of other benzodiazepines. So far there have been only a few controlled clinical trials of Ro 15-1788 in reversing the central effects of benzodiazepines, Jensen *et al.*[5] found a fast awakening, return of orientation in time and space, elimination of amnesia, higher Pa_{O_2} and lower Pa_{CO_2} in patients who received Ro 15-1788 after general anaesthesia with flunitrazepam, fentanyl, pancuronium, N_2O and O_2. Alon *et al.*[6] found an awakening within seconds or a few minutes, return of orientation and abolition of amnesia in patients who received Ro 15-1788 after anaesthesia and midazolam, enflurane, atracurium, N_2O and O_2.

The study reported here showed that Ro 15-1788 effectively antagonised the central effect of diazepam. The degree of sedation was lower in the group treated with Ro 15-1788 than in the control group at all times; the greatest difference was registered at 30 minutes after trial drug administration. Early studies have indicated that the duration of action of Ro 15-1788 is shorter than that of most benzodiazepines. In a study of the effect of Ro 15-1788 during stead state infusion of midazolam in anaesthetic doeses (serum concentration 0.6 μg/ml) all patients who received 10 mg of intravenous Ro 15-1788 were awake within 30–50 seconds, but after an additional 145 minutes they were all asleep again.[7] On the other hand, others[8] found no re-sleep phenomenon in 17 patients sedated for CAT scanning or cystoscopy with midazolam 0.3 mg/kg when the sedation was reversed with Ro 15-1788 in the same dose. We found no sign of returning sedation in the Ro 15-1788 group during the postadministration observation period of 2 hours. After this point, all the patients in both groups were sufficiently awake to be discharged.

In this study Ro 15-1788 was well tolerated and effective in antagonising the central effects of a benzodiazepine sedative. It would appear to have potential in handling the recovery from minor outpatient procedures involving benzodiazepine sedation. In our laboratory we perform 1800 gastroscopies per year, of which approximately 1200 are outpatients. Thus, a safe and effective benzodiazepine antagonist would enable us to reduce the recovery period after the examination by 1.5 hours per patient; this represents a saving of 1800 hours of patient-observation each year. Moreover, benzodiazepines could be used in sufficient doses to assure almost all patients sufficient sedation with amnesia without prolonging recovery.

Acknowledgments

We thank Hoffmann–La Roche for supplying Ro 15-1788 and B.O. Mikkelsen, Clinical Research Department, Hoffman–La Roche for cooperation.

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Anaesthesia, 1986, Volume 41, pages 1189–1195

Glycine and transurethral resection

J.P. ALEXANDER, A. POLLAND AND I.A. GILLESPIE

Summary

Fifty patients undergoing transurethral resection of the prostate were studied for evidence of glycine absorption and haemodilution. Plasma glycine levels increased substantially in nine patients and, in five, calculated irrigant fluid absorption ranged from 619–1582 ml; another patient had absorbed 1360 ml fluid with only a small rise in plasma glycine. Two illustrative case histories are presented. The role of glycine as an inhibitory neurotransmitter is discussed and the possibility of toxic mechanisms other than dilutional hyponatraemia is mentioned. Intravenous diuretics, hypertonic saline, and perhaps calcium salts, are recommended for the overt transurethral resection syndrome.

Key words

Surgery, urological; prostatectomy.
Complications; fluid balance, glycine.

Transurethral resection of the prostate (TURP) is occasionally accompanied by the well-recognised complication known as the TUR syndrome. This is characterised by bradycardia, hypotension (which may be preceded by hypertension), respiratory distress, mental confusion and profound hyponatraemia, and is the result of massive absorption of irrigating fluid, which causes haemodilution. Solutions of 1.5% glycine (which combine good optical, nonelectrolytic and nonhaemolytic properties) are commonly used for irrigation during the operation and may cause problems by intravascular absorption or by extravasation into tissues outside the bladder or prostatic capsule. This study was designed to seek correlations between increases in plasma glycine levels and fluid absorption which may occur during surgery.

Method

Fifty consecutive patients undergoing TURP were studied. Ages ranged from 58–87 years (mean 73 years, SD 7) and body weight from 40–95 kg (mean 68 kg, SD 14). Spinal anaesthesia was employed in 39 patients and general anaesthesia in the remainder. The operative procedures were carried out with intermittent flow resectoscopes (Storz) and the irrigant fluid was 1.5% glycine, with a pressure head approximately 80 cm above the symphysis pubis. The volume of irrigant used and the volume of washings collected were noted and, on completion of surgery, a sample of thoroughly mixed washings was analysed for haemoglobin content using the cyanmethaemoglobin method (Coulter Electronics Ltd Haemoglobinometer). Blood loss cal-

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culations were based on the pre-operative haemoglobin concentrations.

All patients received a slow intravenous infusion of dextran 70 during the procedure and the volume infused was noted (100–200 ml). Venous blood was taken (without the use of a tourniquet) before induction of anaesthesia and again immediately on completion of surgery, for estimation of haemoglobin and haematocrit (Coulter S Plus 4 semi-automated analyser), serum electrolytes (Technicon SMA 11 auto-analyser) and plasma glycine (Goodwin's method which measures total aminoacids).[1] Increases in amino acids in the postoperative samples were confirmed to be due to glycine by high-voltage amino acid electrophoresis. All the laboratory tests are considered to have an accuracy of within 3% in the reference range.

Total red blood cell and plasma volumes were calculated from the pre-operative haematocrit on the assumption that blood volume was 7.5% of body weight. No allowance was made for age, height, obesity or intercurrent disease. Post-operative red cell and plasma volumes were calculated from the change in haematocrit with allowance made for red cell and plasma loss as measured by total blood loss in the TUR washings and the amount of dextran 70 infused (see appendix). The expander index for dextran 70 was assumed to be 1.00, i.e. 30 minutes after the end of the infusion, 100% was assumed to be still within the vascular space.[2] Any increase in calculated plasma volume was considered to represent the minimum volume of glycine solution absorbed by the patient. Absorption of irrigant solution was confirmed by dilution of plasma proteins from pre-operative values.

Results

The majority of our patients tolerated TURP well. However, eight patients developed hypotension (systemic systolic blood pressure ≤ 100 mmHg) during the procedure and in three, spinal anaesthesia seemed to be the only factor responsible. The mean increase in plasma volume overall was 317 ml (SD 423) range −700 to +1582 ml) while increases in plasma glycine levels were unspectacular (mean 1.8 mmol/litre, SD 2.0). However, nine patients had substantial increases in plasma glycine (>7 mmol/litre); in five this was associated with calculated increases in plasma volume of over 500 ml. One further patient (case 32) had a calculated increase in plasma volume of 1360 ml (confirmed by plasma protein dilution) with only a small rise in glycine. Details of these ten patients are listed in Table 1, which also gives changes in serum sodium and potassium.

The weight of prostatic tissue resected ranged from 5–75 g (mean 30 g, SD 20), and the volume of irrigant solution used ranged from 2–20 litres (mean 8 litres, SD 4). A small deficit (0.5–1.7 litres) in the volume of irrigating fluid recovered was noted in only three patients. However, irrigating fluid tends to spill on towels and onto the floor, so that deficits usually only become apparent to the nursing staff when large volumes are involved. Overall, the blood loss ranged from 8–855 ml (mean 200 ml, SD 223), and resection time varied from 20–90 minutes (mean 40, SD 15). Patients who had prolonged resections of large prostates associated with heavy bleeding appeared to be at greater risk of absorbing large amounts of irrigation fluid and of developing high levels of plasma glycine (Table 1).

Case histories

Neither of these case histories occurred in the study patients.

Case 1

A 65-year-old who weighed 95 kg was given anaesthesia by mask for TURP. One hour after completion of resection of 75 g of tissue, which took 1.5 hours, he complained of abdominal pain, became cyanosed with tachypnoea and then comatose with marked limb twitching and a silent distended abdomen. Serum sodium was 109 mmol/litre, calcium 1.8 mmol/litre. After some delay he received 800 ml 5% sodium chloride, frusemide 40 mg and calcium gluconate 20 ml and had a diuresis of 17 litres. His estimated fluid overload was in excess of 10 litres and included 5 litres of intravenous crystalloid solutions. Plasma glycine levels were not measured.

Case 2

A 74-year-old had a TURP performed under spinal anaesthesia. After resection of 55 g of tissue, which took 1.3 hours, he became wheezy and hypotensive and then suffered cardiovascular

Table 1. Laboratory and operation details of nine patients who had large rises in plasma glycine levels and of case 32 who had marked haemodilution with only a small rise in plasma glycine

Case no.	Increase in plasma glycine (mmol/litre)	Increase in plasma volume (ml)	Weight of prostate resected (g)	Operation time (minutes)	Blood loss (ml)	Decrease in serum Na^+ (mmol/litre)	Change in serum K^+ (mmol/litre)	Hypotension systolic BP ≦ 110 mmHg
6	14.8	381	75	60	681	7	−0.7	Yes
11	41	1464	75	70	778	23	+0.5	No
20	10	619	75	70	360	0	0	No
21	8	458	45	50	166	8	+0.3	Yes
22	7.8	0	75	70	596	4	+0.1	Yes
29	16.4	1020	70	70	810	11	+0.2	Yes
32	0.6	1360	40	50	50	1	−0.6	Yes
34	12.9	117	25	30	300	5	+0.8	No
39	10.5	672	20	30	189	5	+0.6	No
40	22.7	1582	40	40	855	12	+0.1	No

collapse. Full resuscitative measures were instituted, which included a short period of external cardiac massage. Serum sodium was 109 mmol/litre. Three litres of irrigation fluid were unaccounted for. He was treated with 50 ml 8.4% sodium bicarbonate, 300 ml 5% sodium chloride and frusemide 40 mg and eventually recovered completely. Plasma glycine one hour postoperatively was 62 mmol/litre and 3 hours later was 44 mmol/litre.

Discussion

The problems of fluid overload and dilutional hyponatraemia during TURP have attracted considerable attention in the literature for the past 40 years,[3-16] and the number of more recent publications on the subject indicates that interest is not waning.[17-32] In addition, new techniques such as percutaneous ultrasonic lithotripsy may also give rise to extravasation and hyponatraemia.[33] Our method of calculating plasma volume expansion from haematocrit dilution, and hence deriving fluid absorption, is subject to a number of possible inaccuracies.[34] However, we are left with the conclusion that in some patients undergoing TURP, there is a considerable rise in plasma glycine which may be accompanied by a marked fall in haematocrit. Both water and glycine are freely distributed through the extracellular space, and probably the intracellular space, and it seems likely that serum glycine represents only some 40% of that absorbed.[18] Investigations using a double isotope technique indicated that the speed of fluid absorption was related to the pressure head of the irrigation fluid, of which a considerable amount can be absorbed extravascularly through defects in the prostatic capsule.[13] Estimates of the rate at which fluid can enter the circulation through open prostatic venous sinuses vary from an average 20 ml/minute of resection time[4] to an exceptional 87 ml/minute.[7] The calculated total amounts of fluid absorbed in two fatal cases (based on serum sodium dilution) were 3 and 6 litres respectively.[15]

Figure 1 shows poor correlation overall between increases in plasma glycine and calculated fluid absorption. Where large amounts were absorbed, there was relatively good correlation between the two (Fig. 2).

Case 2 is included in Fig. 2 since a known amount of irrigation fluid was lost; he also illustrates the fact that when body compartments become saturated with glycine, high plasma levels may be maintained for a considerable time. Since oxalate is a metabolic product of glycine, hyperoxaluria and raised urinary glycolate may constitute a hazard to the kidneys.[24]

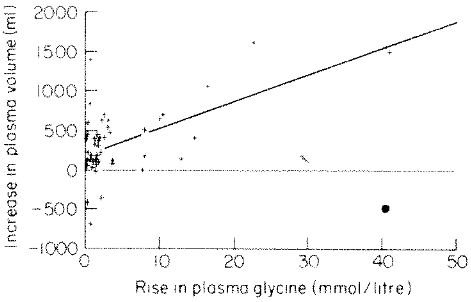

Fig. 1. Relation between increase in plasma glycine and calculated increase in plasma volume in 50 patients. The majority of patients have only a small increase in glycine levels. The equation for the straight line is $y = 34x + 177$ and $r = 0.58$.

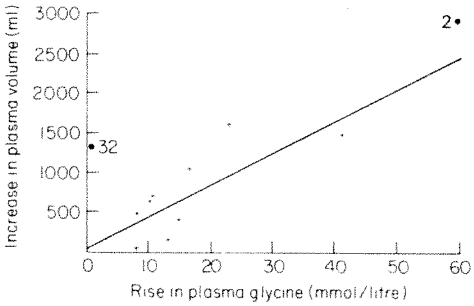

Fig. 2. Relation between increase in plasma glycine and calculated increase in plasma volume in nine patients who had large increases in plasma glycine. The equation for the line is $y = 41x + 52$ and $r = 0.77$. Case 32 and case 2 are inserted as solid circles.

In addition to hyponatraemia, transient hyperkalaemia has been noted in experimental infusion of glycine in humans.[30] Hyperkalaemia has rarely been a feature of clinical reports and was not a consistent finding in our investigation (Table 1). Serum calcium ion levels are not monitored routinely, but calcium salts given intravenously may be effective in treating the sudden cardiovascular collapse associated with the TUR syndrome.[20,30,32] The simplistic view ascribes the TUR syndrome to intravascular absorption of irrigant fluid, leading to water intoxication and dilutional hyponatraemia. This may not be the entire explanation. Zucker and Bull[35] discussed the implications of combined intravascular and extravascular (perivesicular) absorption of bladder irrigation fluid and suggested that dilutional hyponatraemia should be viewed as a separate entity from acute water intoxication. These authors postulate that, under certain circumstances, water from the moderately hypo-osmolar bladder irrigation fluid may diffuse into the intravascular compartment from the perivesicular and retroperitoneal tissues at a greater rate than the osmotically active glycine molecules. Sodium ions may diffuse in the opposite direction, out of the vascular compartment. They described a case where water intoxication with hyponatraemia occurred with very little change in plasma glycine, similar in some respects to case 32 (Table 1).

By contrast, intravascular infusion of glycine is likely to produce rapid increases in plasma levels of amino acid, without necessarily profoundly affecting sodium ion levels. Glycine infused at rates in excess of 5.3 mg/kg/minute was invariably lethal in dogs,[35] and this rate of infusion is only 25% greater than the mean rate of intravascular absorption found by Hagstrom,[4] which may in some cases be exceeded several-fold.[7] A total dose of glycine of 372.9 mg/kg produced malaise and nausea in man;[35] this is equivalent to the absorption of 1.74 litres of irrigant in the average sized male.

Glycine is now recognised to be an inhibitory neurotransmitter in the mammalian central nervous system, where it acts in the same manner as gamma-aminobutyric acid on chloride ion channels.[36] The majority of these receptors are in the spinal cord, brain stem, diencephalon and retina. The benzodiazepine drugs mimic glycine neurophysiologically, an effect shared to a limited extent by serine, a metabolite of glycine. Experiments in animals indicate that glycine receptors are profoundly influenced by alterations in extracellular and intracellular concentrations of chloride and perhaps other ions.[37–40] Ovassapian *et al.*[41] described five cases of temporary visual disturbance after TURP, thought to be due to interruption of retinal synapses by high glycine concentrations. Others[42,43] have identified ammonia as a toxic metabolite of glycine metabolism and have implicated other possible harmful breakdown products.[35]

It seems possible that several mechanisms may be responsible for the TUR syndrome but, whatever the explanation, a number of measures may be useful in prevention. A high level of suspicion should be maintained. The height of the reservoir bag above the symphysis pubis should be kept to a minimum; 60 cm has been recommended but may not give adequate flows to keep the visual field of the resectionist clear. The reservoir height should never exceed 100 cm. Spinal anaesthesia with minimal sedation allows early recognition of respiratory distress or cerebral irritation and confusion. The three risk factors of prolonged resection, large prostate and profuse bleeding were present in five of our nine patients who absorbed large amounts of glycine and one factor was present in another such patient.

Central venous pressure monitoring may show a rapid rise in central venous pressure when fluid absorption occurs.[12] Infusion of intravenous fluids should be kept to a minimum. Continuous monitoring of plasma sodium using an intravascular ion selective electrode has been described.[28] Patients with pre-operative hyponatraemia are at great risk of cardiovascular collapse and death.[15]

Where the TUR syndrome does occur, diuretics and hypertonic saline should be administered early, although the use of the latter still seems to be controversial.[44] However, there does appear to be a subgroup of patients who are incapable of excreting a water load where serum sodium levels remain low,[4,5,8,18,32] and if cardiovascular collapse occurs, intravenous calcium salts may be helpful.

Acknowledgments

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Appendix

$$\text{Blood loss (BL) (ml)} = \frac{\text{Haemoglobin (Hb) in washings (g/dlitre)} \times \text{volume of washings (ml)}}{\text{patient's Hb (g/dlitre)}}$$

$BV^* = \text{wt (kg)} \times 75 \text{ ml}$

$RCV^* = BV^* \times PCV^* \text{ (ratio)}$

$PV^* = BV^* - RCV^*$

$RCL = BL \times PCV^*$

$PL = BL - RCL$

$RCV^\dagger = RCV^* - RCL$

$BV^\dagger = \dfrac{RCV^\dagger}{PCV^\dagger}$

$PV^\dagger = BV^\dagger - RCV^\dagger$

Expansion of plasma volume = $PV^\dagger - (PV^* - PL) - D70$

By substitution this can be written

$$\left[\frac{RCV^* - (BL \times PCV^*)}{PCV^\dagger}\right] - [RCV^* - (BL \times PCV^*)]$$

$$- [(BV^* - RCV^*) - [BL - (BL \times PCV^*]] - D70$$

BV = blood volume (ml), RCV = red cell volume, PCV = haematocrit, Hb = haemoglobin,
PV = plasma volume, RCL = red cell loss,
BL = blood loss, PL = plasma loss, D70 = volume of dextran 70 infused,* and † indicate pre- and postoperative values respectively. Calculations were performed on an HP – 97 Programmable Printing Calculator (Hewlett-Packard).

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Intravenous regional anaesthesia below the knee

A cross-over study with prilocaine in volunteers

H. VALLI AND P. H. ROSENBERG

Summary

The quality of anaesthesia provided by three dosages of prilocaine, 40 ml 0.5%, 20 ml 1%, or 40 ml 1%, administered in random order, for intravenous regional anaesthesia of the lower extremity below the knee was compared in six volunteers. Limited sensory blockade was achieved in the groups with 40 ml 0.5% and 20 ml 1% during the 30-minute test period. One subject was not fully anaesthetised with any of the dosages used. Recovery was rapid (mean 12–13 minutes) in these two groups. In two subjects given 40 ml of 1%, complete recovery took 90 minutes. At 30 minutes, the degree of flexion remaining in the great toe (control 100%) was 4% in the groups who received 40 ml of 0.5% and 1%, but 34% in those who received 20 ml of 1% respectively. Full motor recovery was achieved in 8–9 minutes. Five of six volunteers who received the 400-mg dose experienced subjective signs of central nervous system side effects when the cuff was released. In this group, the mean plasma level of prilocaine at 2 minutes was 1.22 μg/ml, maximum 2.12 μg/ml. In a radiological examination, no leak of contrast medium under the tourniquet cuff (300 mmHg) was detected. The development of anaesthesia was fastest following the largest dose, but the large number of central side effects makes that dosage less suitable for clinical work.

Key words

Anaesthetic techniques, regional; intravenous regional.
Anaesthetics, local; prilocaine.

Intravenous regional anaesthesia (IVRA) of the leg below the knee has been suggested as a suitable technique for short-lasting outpatient surgery of the foot and ankle.[1,2] Controlled studies regarding the dosage of local anaesthetic used and the efficacy of the block are apparently lacking. Therefore, considering the principles employed for IVRA of the arm, a cross-over study was designed, using volunteers who received three different solutions of prilocaine for IVRA. Prilocaine was chosen because its safety when used in IVRA of the arm has been well documented.[3,4]

Methods

The study was approved by the ethics committee of the hospital. Six healthy male volunteer anaesthetists aged between 28 and 41 years and weighing between 68 and 90 kg took part in the cross-over study. Chest electrodes were applied for continuous ECG monitoring. Arterial blood pressure and heart rate were recorded using an automatic device. An indwelling cannula was inserted in an antecubital vein and an infusion of Ringer's solution started.

A 1.2-mm cannula was placed into a vein on the dorsum of the foot. The leg to be studied was comfortably positioned on pillows with the knee slightly flexed. Two cuffs, each 7 cm wide, were placed around the calf and the foot which was then exsanguinated using a rubber Esmarch bandage. The proximal tourniquet cuff was inflated to 150 mmHg over the volunteer's control systolic blood pressure, or to a minimum of 280 mmHg. On four occasions (two subjects)

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a cuff pressure of 350 mmHg was required to prevent arterial inflow. It was planned to switch the pressure from the proximal to the distal cuff after 15 minutes. The tourniquet time was 30 minutes.

A nonelastic string was attached with tape to the distal phalanx of the big toe. At an angle of approximately 45 degrees to the longitudinal axis of the horizontally lying subject, the string was connected to a spring balance of 1 kg capacity; flexion of the toe produced a reading on the scale. The pre-tension was adjusted to 300 g and the 100% point was taken as the degree of flexion on the scale produced before the start of the test. At intervals of at least 3 days apart, IVRA was performed at random with either 40 ml of 0.5% prilocaine (group 1), 20 ml of 1% prilocaine (group 2) or 40 ml 1% prilocaine (group 3), injected at a rate of 20 ml/minute into the vein on the dorsum of the foot. Skin sensation to pin prick, tested with a 27-gauge needle, was estimated at 2-minute intervals as follows: sharp changing to blunt was recorded as analgesia; no sensation indicated anaesthesia. The tests were carried out in three areas: tibial nerve (the front region of the plantar side of the foot), deep peroneal nerve (between the first and second toe) and superficial peroneal nerve (dorsum of the foot, near the ankle).

Flexion of the big toe was also measured at 2-minutes. If necessary, testing of pinprick sensa- the tourniquet was inflated. After cuff deflation, testing of recovery of sensory and motor function was performed at 2-minute intervals for 30 minutes. If necessary, testing of pin prick sensation was continued at 15-minute intervals until complete recovery. Subjective symptoms experienced by the volunteers were recorded.

Five millilitres of blood were withdrawn into heparinised tubes before the start of the experiment, prior to deflation of the tourniquet and at 2, 5, 10, 20, and 30 minutes after releasing the tourniquet. The blood samples were centrifuged and the plasma removed and stored at − 70°C until prilocaine levels were determined by gas chromatography according to Mather and Tucker.[5]

To test the effect of ischaemia as a component of IVRA, three of the volunteers received 40 ml of 0.9% NaCl; the method of testing was as described above. Three volunteers also underwent a phlebographic examination using a similar method to that for IVRA. Instead of the local anaesthetic, 40 ml of contrast medium was injected and eight radiographs were taken at 30-second intervals.

Statistical significance was evaluated through pairwise comparison using a two-tailed t-test for dependent samples. A binomial distribution test was used to test the recovery times, which did not follow a normal distribution.

Results

Sensory testing

The results of pinprick testing at the three different skin spots are shown in Table 1. In one subject, no analgesia in the area of the superficial peroneal nerve was achieved with the use of solutions 1 and 2 and there was no anaesthesia with any of the solutions.

There was no significant difference between groups as regards the times taken to the onset of analgesia. Group 3 achieved anaesthesia significantly faster than group 2 ($p < 0.01$, $p = 0.001$, $p = 0.008$ for different nerve spots). The only significant difference between groups 1 and 2 was achieved in the area of the tibial nerve ($p = 0.015$).

All the volunteers felt pressure under the cuff and in two subjects, inflation of the distal cuff became intolerable so that the proximal one had to be refilled and used throughout the rest of the procedure. On average, the skin spot representing the superficial peroneal nerve recovered far more rapidly ($p = 0.075$). With solutions 1 and 2, mean full recovery of sensation occurred in 3 minutes, while the other skin spots took significantly longer. The longest sensory recovery in the study was in group 3, where two of the volunteers did not recover completely for more than 90 minutes. Recovery was significantly faster ($p < 0.05$) in groups 1 and 2 than in group 3. There was no difference between the first two groups.

Motor testing

The mean flexion ability of the big toe 30 minutes after the injection had decreased from 100% to 4% (SD 7%) in group 1, to 34% (SD 36%) in group 2 and to 4% (SD 5%) in group 3. On average, full motor recovery occurred after some 8–9 minutes, except for one volunteer in group 3, whose recovery was only to the 90% level in 30 minutes, at which time motor testing was ended.

Table 1. Mean times (minutes, SD) to establish analgesia, anaesthesia and recovery

	Analgesia			Anaesthesia			Recovery		
	1	2	3	1	2	3	1	2	3
Tibial nerve	6.7 (4.7)	7.3 (2.3)	3.7 (2.3)	14.3 (2.3)	16 (4.6)	10 (2.8)	11.5 (16.9)	10.7 (10)	26.2 (35.5)
Deep peroneal nerve	5.0 (3.0)	9.3 (6.3)	5.0 (3.5)	13.7 (2.9)	17.3 (3.3)	9.7 (4.1)	10.8 (16.9)	13.3 (23.1)	28.0 (35.3)
Superficial peroneal nerve*	8.8 (4.6)	14.8 (6.1)	9.0 (6.5)	13.6 (4.8)	18.4 (3.3)	9.6 (2.6)	2.7 (1.6)	2.7 (1.7)	16.8 (18.8)

*One subject had incomplete analgesia and no anaesthesia.

Central nervous system symptoms and prilocaine plasma concentrations

In group 3, on releasing the tourniquet, five of the volunteers experienced symptoms of mild central nervous system (CNS) intoxication, such as tinnitus, lightheadedness, numbness of the lips and at the tip of the tongue. The sixth volunteer, when injected with the largest dose, had similar symptoms, immediately the injection was completed. However, just before releasing the tourniquet at 30 minutes, no prilocaine was demonstrated in his plasma. One subject in group 1 and two in group 2 had mild CNS toxicity symptoms when the tourniquet was deflated. The CNS symptoms began between 1.5–3 minutes after release of the tourniquet and lasted for about 6–8 minutes.

The mean and individual venous plasma concentrations are shown in Figs 1 and 2. There was no correlation between the dose on a weight basis and the plasma concentration of prilocaine. One of the subjects (4) had a leakage of the local anaesthetic under the tourniquet. The prilocaine level in the plasma immediately before deflation of the tourniquet was 0.44 μg/ml.

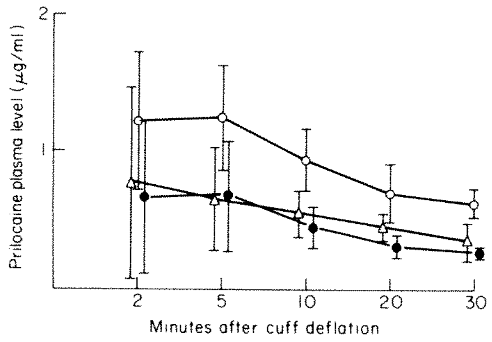

Fig. 1. Mean plasma concentrations (μg/ml, SD) of prilocaine in six volunteers in association with intravenous regional anaesthesia below the knee. ●, 40 ml 0.5%; △, 20 ml 1%; ○, 40 ml 1%.

In the subject with incomplete analgesia (6), the first sample after tourniquet deflation on each occasion contained quite a high concentration of prilocaine (Fig. 2). In the three subjects who experienced mild CNS toxicity symptoms at cuff deflation when the lower doses of prilocaine had been injected (groups 1 and 2), the mean plasma concentrations of prilocaine at 2 and 5 minutes were not significantly different from those in the subjects who remained symptomless.

Circulation

Blood pressure and heart rate remained virtually unchanged during the study in all volunteers.

Tourniquet pain

In two of the volunteers the planned switch of the pressure from the proximal to the distal cuff at 15 minutes caused intense pain. In one subject this occurred in association with solution 3 and in the other when both solutions 1 and 2 were used. In all cases, tourniquet pressure was felt throughout the anaesthetic procedure.

Saline study

The mean latency of analgesia at the skin area representing the deep tibial nerve was 7.3 minutes (SD 5.0) and that of anaesthesia 18 minutes (SD 20). Mean recovery time was 6 minutes (SD (5.3). Only one subject had any analgesia at the skin area innervated by the deep peroneal nerve. At the area of the superficial peroneal nerve, all perceived the pinprick as being sharp, although the sensation was weaker than normal and burning in character. Thirty minutes after the saline injection, the remaining flexion ability of the big toe was 53% (SD 46%).

Radiographic examination

There was no leak of contrast medium under the tourniquet during the 4 minutes following the injection.

Discussion

In five of the six volunteers, surgery of the foot would probably have been possible without pain within the study period of 30 minutes after injection of 200 mg of prilocaine (20 or 40 ml). The sixth volunteer was clearly different from the others in that with the larger dose of 400 mg prilocaine there was not complete anaesthesia in all three skin test spots by 30 minutes. Interestingly, he had consistently high plasma concentrations of prilocaine immediately after tourniquet cuff release, which suggests that a large portion of the local anaesthetic had escaped from

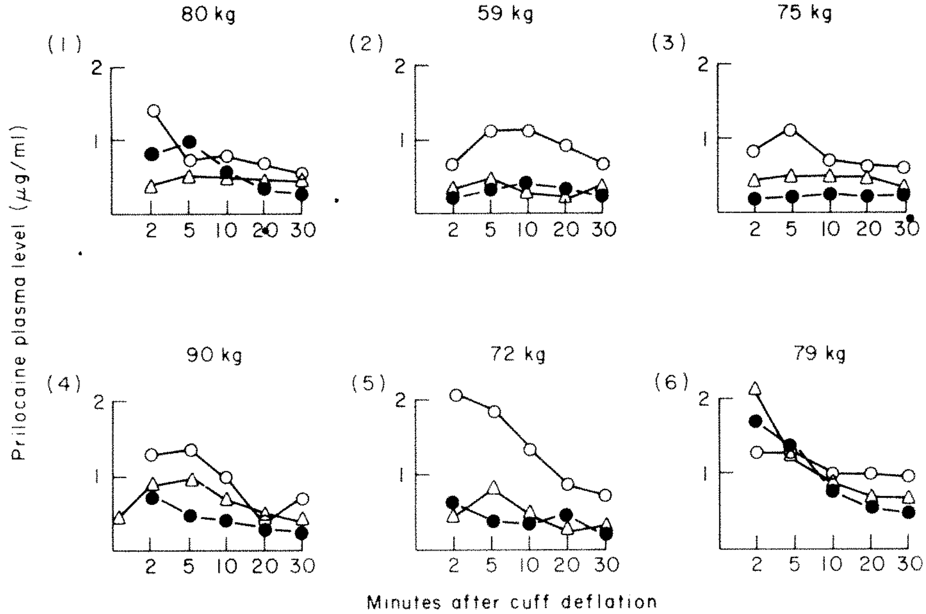

Fig. 2. Individual plasma concentrations (μg/ml) of prilocaine in six volunteers. ●, 40 ml 0.5%; △, 20 ml 1%; ○, 40 ml 1%.

the site of action and remained in larger veins, resulting in rapid washout of prilocaine.

The volume of the anaesthetic solution seemed to be an important determinant in the development of the motor block. Forty millilitres of 1% solution produced a motor block equivalent to that of 40 ml 0.5% prilocaine, while half the volume containing the smaller dose was clearly inferior in blocking flexion of the great toe. It may be speculated that 20 ml is too small a volume to fill the venous channels within the larger nerve trunks,[6] thus preventing the development of profound motor block. On the other hand, as the onset of analgesia during an IVRA may depend to a great extent on the anaesthetic solution reaching peripheral nerve endings,[7] the smaller volume of the foot seems to allow easy filling of the superficial venous network of the foot.

Ischaemia has an additive effect on the IVRA produced by the local anaesthetic.[8] Interestingly enough, in this study, the skin area representing the deep tibial nerve was blocked as rapidly by using 200 mg prilocaine as by ischaemia alone (40 ml of saline). In contrast, at the other two skin areas, no anaesthesia was seen by 30 minutes. There was also a clear difference in the motor block, which was significantly more intense with the use of local anaesthetic than without it. Notably, in approximately similar conditions, ischaemia (saline IVRA) of the arm resulted in complete motor block (finger flexion) within 21 minutes.[8] The difference in latency and degree of motor block of the hand and foot by ischaemia may depend on the amount of muscle mass distal to the tourniquet.

The fact that both sensory and motor recovery was quite long after the use of the larger dose of prilocaine, strongly supports the view that concentrated solutions of local anaesthetics in IVRA of the arm produce prolonged post deflation analgesia[9] and the speculation that the site of action is on large nerve trunks.[6]

The venous plasma concentrations of prilocaine after tourniquet release seemed to be independent of injected dose per unit weight and, furthermore, the occurrence of CNS symptoms did not correlate with the prilocaine levels in the volunteers with CNS symptoms; at 2 minutes the lowest plasma level was 0.47 μg/ml, and the highest 2.12 μg/ml. Lack of correlation between venous local anaesthetic levels and toxic symptoms is in agreement with earlier studies.[10] It has been suggested that latent anxiety and differences in pain threshold could influence the development of CNS intoxication by local anaesthetics.[11] However, the major factor causing great individual variations in plasma levels is probably difference in redistribution and the result of a significant uptake of prilocaine by the lungs, even during the first passage.[12] The mode of tourniquet cuff release, sudden versus intermittent, may not affect the venous levels of prilocaine in IVRA of the lower leg. In IVRA of the arm, the mode of tourniquet release does not influence the levels of lignocaine[13] and bupivacaine.[14]

One of the volunteers, on one occasion, had prilocaine in his circulation before the cuff was deflated, which suggests that normally the 7-cm wide cuff at a pressure of 280–350 mmHg around the calf prevents leakage of the local anaesthetic from the exsanguinated area. This was confirmed in the radiographic examination where 300 mmHg pressure clearly withheld the injection pressure and the pressure created by 40 ml contrast solution filling the veins distal to the cuff. In contrast to the situation in IVRA of the arm, where switching pressure to the more distal tourniquet after approximately 15 minutes usually eases tourniquet pain, this seems not always to be the case in IVRA of the lower leg. Two subjects preferred to have the pressure remain in the proximal cuff due to insufficient analgesia under the distal one.

In conclusion, IVRA below the knee with prilocaine in doses of 200 or 400 mg and volumes of 20 or 40 ml, produced varying degrees of sensory and motor blockade of the foot. The larger volume of local anaesthetic enhanced the efficacy of the motor block. With 200 mg, the development of sensory blockade would probably be too slow for busy outpatient surgery programmes. With the 400 mg dose, the block was rapid, but toxic symptoms occurred frequently when the cuff was deflated. Considering these relative limitations, the technique can be recommended using prilocaine for outpatient surgery. For safety reasons, the block should be administered by anaesthetists who are fully versed in the recognition and management of toxic reactions to local anaesthetics.

Acknowledgements

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Anaesthesia, 1986, Volume 41, pages 1202–1206

Combination treatment with ranitidine and sodium bicarbonate prior to obstetric anaesthesia

H. M. L. MATHEWS, C. M. WILSON, E. M. THOMPSON AND J. MOORE

Summary

The gastric pH and volume were measured in 175 patients undergoing elective, and 313 undergoing emergency, obstetric procedures. Ranitidine 150 mg was administered orally every 6 hours in labour and at least 2 hours before elective Caesarean section. Patients received 20 ml of 8.4% sodium bicarbonate orally immediately prior to induction of anaesthesia. The combination of ranitidine and sodium bicarbonate produced marked alkalinisation of gastric contents (mean pH 8.9). The administration of sodium bicarbonate pre-operatively in patients who received ranitidine less than 2 hours before operation led to satisfactory elevation of gastric pH. Only four patients had a gastric pH < 2.5, one patient refused any medication, two received only ranitidine and one patient had a long interval from administration of bicarbonate to aspiration of gastric contents. Gastric volumes were high in labouring patients (mean 84 ml) despite administration of ranitidine. The effectiveness of sodium bicarbonate as a single dose antacid therapy prior to obstetric anaesthesia requires further study.

Key words

Gastrointestinal tract; stomach, pH, volume.
Histamine; H_2-receptor antagonist, ranitidine.
Pharmacology; sodium bicarbonate.

Ranitidine 150 mg given orally every 6 hours during labour is ineffective in raising the gastric pH in 100% of women.[1] Some patients may require an emergency general anaesthetic within 2 hours of administration of the ranitidine and this does not give sufficient time for emptying of existing acid present in the stomach and the achievement of adequate therapeutic levels of the drug. Furthermore, patients in labour who are receiving opioids will have delayed stomach emptying and less absorption of ranitidine. It is thus advisable to supplement ranitidine with a pre-anaesthetic antacid. This paper reports a study of the use of oral ranitidine supplemented by an oral dose of 20 ml 8.4% sodium bicarbonate immediately before general anaesthesia. In an unpublished pilot study the authors have demonstrated the effective, but brief, neutralising ability of this dose of antacid.

Method

All patients admitted to the delivery ward in labour were given a tablet of ranitidine 150 mg

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orally every 6 hours. Those for elective Caesarean section received only one tablet, given at least 2 hours before operation. Both groups received 20 ml 8.4% sodium bicarbonate immediately prior to pre-oxygenation, usually within 5 minutes and all within 15 minutes of induction of anaesthesia.

All patients were anaesthetised using a technique involving pre-oxygenation, rapid intravenous induction, application of cricoid pressure and muscle relaxation followed by tracheal intubation. When anaesthesia was established, a lightly lubricated No. 18 Salem sump tube was introduced into the stomach, via a 7.5 uncuffed orotracheal tube placed in the oesophagus, until only the last 10 cm remained visible. Aspiration of stomach contents was performed during its slow withdrawal. The volume of contents was measured and the pH determined using a Corning 113 pH meter and microelectrode.

The times from administration of ranitidine to induction of anaesthesia, administration of bicarbonate to induction and administration of bicarbonate to aspiration of stomach contents were all recorded, as well as the number of ranitidine tablets which the patient received.

Results

The volume and pH of aspirated gastric contents were measured in a total of 175 patients undergoing elective and 313 undergoing emergency procedures. Table 1 shows the mean gastric pH and volume in those patients who received ranitidine according to the protocol. In an additional two patients in the elective group, we were unable to obtain any gastric aspirate. In no patient in either group was the gastric pH under 2.5, but on occasions it was as high as 10.0.

Table 1. Mean (SEM) with range of gastric pH and volume in patients who received ranitidine 2–6 hours before induction of anaesthesia in combination with sodium bicarbonate less than 15 minutes before induction

	n	pH	Volume (ml)
Elective	118	8.9 (0.06) (6.1–10.0)	30.0 (1.45) 1.0–80.0)
Emergency	217	8.4 (0.07) (3.8–9.8)	84.2 (6.54) (1.5–550.0)

Table 2 shows findings in patients who received an anaesthetic within 2 hours of ranitidine. In all cases, the pre-anaesthetic administration of sodium bicarbonate led to satisfactory elevation of gastric pH, although in emergency cases the mean pH was significantly ($p < 0.05$) less than in Table 1. Seventeen patients in labour required anaesthesia more than 6 hours from the last dose of ranitidine. The administration of sodium bicarbonate again ensured that all had satisfactory elevation of gastric pH (mean 8.2, SEM 0.22, range 6.1–9.3).

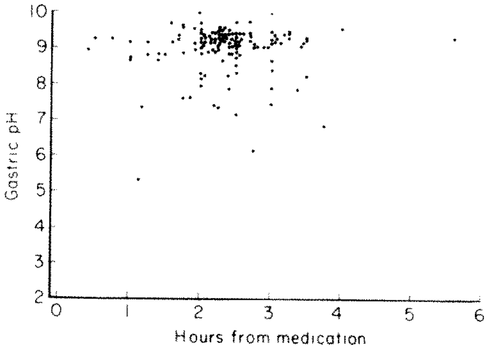

Fig. 1. pH of gastric contents from 175 women undergoing elective Caesarean section who received 150 mg ranitidine supplemented with 20 ml 8.4% sodium bicarbonate less than 15 minutes before induction of anaesthesia.

Figure 1 shows the pH scatter in patients for elective Caesarean section illustrating the high values obtained in this group. This includes the patients in Tables 1 and 2. Figure 2 shows the scatter in the emergency cases given only one tablet of ranitidine. There is a wider scatter of pH values during the first 2-hour period.

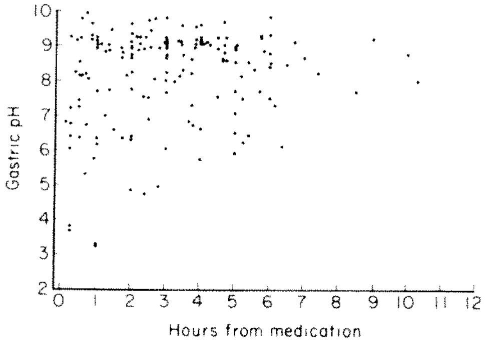

Fig. 2. pH of gastric contents from 313 women in labour who received ranitidine 150 mg supplemented with 20 ml 18.4% sodium bicarbonate less than 15 minutes before induction of anaesthesia.

Table 2. Mean (SEM) with range of gastric pH and volume in patients who received ranitidine less than 2 hours before anaesthesia. Sodium bicarbonate given less than 15 minutes before induction of anaesthesia

	n	pH	Volume (ml)
Elective	27	8.9 (0.11) (7.3–10.0)	36.3 (5.54) (1.0–125.0)
Emergency	45	7.8 (0.25) (3.2–9.9)	62.9 (8.94) (1.5–300.0)

Table 3. Mean (SEM) with range of gastric pH and volume in patients who received ranitidine 2–6 hours before induction of anaesthesia. Administration of bicarbonate–aspiration time was more than 20 minutes

	n	pH	Volume (ml)
Elective	22	8.8 (0.15) (6.6–9.5)	29.9 (3.91) (1.0–66.0)
Emergency	24	8.4 (0.17) (6.9–9.3)	87.7 (13.55) (3.3–240.0)

Table 3 shows the results when stomach contents were aspirated more than 20 minutes after administration of bicarbonate. Again, there was satisfactory elevation of gastric pH and, in one additional emergency patient, no aspirate was obtained.

Four patients who were having emergency operations received ranitidine less than 2 hours before operation. In one patient the bicarbonate to aspiration interval was 27 minutes and the pH was 1.7; in the other three patients the mean bicarbonate–aspiration interval was 37 minutes and the pH ranged from 6.7–8.2. Three patients who were having elective procedures given ranitidine less than 2 hours before operation (mean bicarbonate–aspiration time 28 minutes) had pH values ranging from 7.6–9.0.

Table 4 shows the gastric pH values in those patients who did not receive the combination of ranitidine and bicarbonate. Two patients who received only ranitidine and one patient who received no antacid therapy had pH values of less than 2.5.

Discussion

One could criticise this paper because of the use of mean pH readings, since these are derived non-linear values.[2] However, this is considered an accepted method of presenting results.[3]

The two patients with gastric pH less than 2.5 who received only ranitidine emphasise again the inadequacy of ranitidine as the sole antacid in labour. All patients in labour who received ranitidine 2–6 hours before operation in combination with bicarbonate immediately before induction of anaesthesia had satisfactory elevation of gastric pH, covering both induction of and emergence from anaesthesia. Those patients in labour who received ranitidine less than 2 hours before operation in combination with bicarbonate also had adequate but significantly less elevation of gastric pH at induction of anaesthesia.

The findings in the only patient who received bicarbonate and had an unacceptable gastric acidity may be explained by the long interval from administration of bicarbonate to aspiration (27 minutes), again emphasising the brief neutralising action of bicarbonate. In our pilot study, rebound acidity was demonstrated in a group of 12 gynaecological patients given bicarbonate 1 hour pre-operatively; gastric pH was less than 2.5 in 11 patients, as compared with 56% of a control group who received no alkali. These findings are similar to the *in vitro* study of Lahiri *et al.*[4] By contrast, Lim and Tan[5] treated 55 emergency obstetric patients with an immediate pre-anaesthetic dose of 20 ml 8.4% sodium bicarbonate and found that the lowest intragastric pH was 6.84 and that its duration of

Table 4. Gastric pH in patients who did not receive the combination of ranitidine and bicarbonate

Antacid therapy	Procedure	pH
Ranitidine only 2 hours pre-operatively	Emergency	1.08
Ranitidine only 3 hours pre-operatively	Emergency	1.66
Rantitidine only 2+ hours pre-operatively, 3 patients	Elective	7.53 8.12 3.03
Bicarbonate only		
Administration–aspiration interval 20 minutes	Emergency	9.08
Administration–aspiration interval 75 minutes	Emergency	7.50
No antacid therapy	Emergency	1.08

action was sufficient to cover the period of emergence. The duration and effectiveness of sodium bicarbonate as a sole pre-anaesthetic antacid in labouring patients are worthy of further study, particularly as we have produced marked alkalinisation of stomach contents with the combination of ranitidine and sodium bicarbonate.

In dogs, Gibbs *et al.*[6] showed that the particulate nature, rather than the alkalinity, of an emulsion antacid produced lung damage when aspirated. Sodium bicarbonate is a nonemulsion saline antacid. However, it would seem sensible that antacid therapy should achieve neutral rather than alkaline gastric contents. The stomach contents were significantly less alkaline (mean pH 7.8) in the group of patients who could be considered as having only bicarbonate, since anaesthesia was induced within 2 hours of administration of ranitidine. Not only is sodium bicarbonate a very effective antacid, but it also mixes well with stomach contents.[7] It reacts with hydrochloric acid to form NaCl, H_2O and CO_2. Twenty millilitres of 8.4% sodium bicarbonate will evolve 509 ml of CO_2 gas, which might theoretically increase the risk of regurgitation during induction; however, this was not a problem in our study.

The situation in patients undergoing elective Caesarean section is quite different. Ranitidine, when given at least 2 hours before induction of anaesthesia, is sufficient to produce reliable, safe intragastric conditions.[8] The mean intragastric pH in our elective cases given ranitidine and sodium bicarbonate is alkaline (8.9) and the mean volume of 30 ml suggests that most of the intragastric volume consists of the previously administered solution of sodium bicarbonate. We therefore recommend that, provided ranitidine is given at least 2 hours before elective Caesarean section, bicarbonate therapy is not only unnecessary, but may be hazardous by increasing the volume of stomach contents.

Roberts and Shirley,[9] using data obtained from animal experiments, arbitrarily defined the patient at risk as having at least 25 ml of gastric contents of pH below 2.5. The mean intragastric volume of 84 ml found in labouring patients is high, although the range (1–550 ml) was considerable. In only 24% of patients was the volume of gastric contents 25 ml or less and 27% of patients had volumes in excess of 100 ml.

Holdsworth[10] found that labouring patients who received opioids had the highest intragastric volume (mean 122 ml) as compared with those patients in whom pain was obtunded by an epidural block (mean 50 ml). Unfortunately, in our study, data are not available to correlate the findings with the use of epidural or opioid analgesia and our mean volume is based on all cases. Ranitidine, by decreasing acid production, should reduce the volume of stomach contents, although in this study some patients had remarkably high volumes. Previous work from this department has shown that ranitidine decreases intragastric volume in patients undergoing elective Caesarean section.[8] Its use in labour resulted in lower volumes when compared with patients receiving regular 2-hourly administration of mist magnesium trisilicate BP.[1]

Further study of the effect on gastric pH and volume of a single pre-anaesthetic dose of sodium bicarbonate is indicated in patients with and without background ranitidine treatment. If the saline antacid alone proves effective, then one can only continue to justify the use of ranitidine in labour if it proves to have a significant effect in decreasing the volume of gastric contents.

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A double-blind comparison of intramuscular pethidine and nalbuphine in labour

C. M. WILSON, E. McCLEAN, J. MOORE AND J. W. DUNDEE

Summary

A double-blind, between-patient comparison of intramuscular pethidine 100 mg and nalbuphine 20 mg for the relief of pain during labour in 80 patients is described. Severity of pain was assessed before and after treatment by subjective pain scores and visual analogue scales. Neither of these methods showed a significant difference between the treatments. Nalbuphine was associated with less maternal nausea and vomiting than pethidine, but this possible advantage was somewhat offset by a tendency of the drug to produce more maternal sedation and dizziness. The mean umbilical vein/maternal vein ratio was significantly higher for nalbuphine (0.78, SEM 0.03) than for pethidine (0.61, SEM 0.02), which suggests easier placental transfer of the former. This finding was reflected in significantly lower 2–4 hour neurobehavioural scores for the infants of mothers given nalbuphine, but there was no significant difference between these scores at 24 hours. On the basis of this study, nalbuphine does not offer a substantial improvement over pethidine for pain relief in labour.

Key words

Obstetric anaesthesia; analgesia.
Analgesics, narcotic; pethidine, nalbuphine.

Despite the increase in the use of regional analgesia for pain relief in obstetrics, the vast majority of women still have to rely on intramuscular opioid analgesia. A recently published retrospective survey reported that between 1970 and 1974, 87% of patients had conventional analgesia. This had fallen to 77% for the years 1975 to 1979. There was also an improvement in reported Apgar scores in the later period, probably due to the lower doses of pethidine being used.[1]

An investigation into pain experienced by women in labour, as assessed by interview 48 hours after delivery,[2] showed that 72% of patients who had received epidural analgesia and 70% of women who received parenteral analgesics or nitrous oxide–oxygen claimed that they had only as much pain as they expected. Therefore, despite excellent analgesia afforded by epidural blockade, many women are satisfied with intramuscular treatment and accept its associated low degree of pain relief.

Pethidine is still the drug of choice in British obstetric practice, even though its use can be associated with nausea and vomiting in as many as 50% of patients[3,4] and occasionally,

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after its intramuscular injection, with maternal hypoxaemia[5] and fetal heart rate decelerations.[6] Equally importantly, following transplacental passage, the infant is limited in its ability to metabolise pethidine and this leads to accumulation[7] resulting in a prolonged (23 hours) elimination half-life in the neonate.[8] Even in moderate maternal dosage (mean 105 mg), pethidine adversely affects infant neurobehaviour.[9]

Any new drug likely to supersede pethidine as an analgesic in labour must produce at least equivalent pain relief with fewer unwanted effects. Nalbuphine, a new semi-synthetic narcotic agonist–antagonist analgesic of the phenanthrene series, has been recommended for the relief of moderate to severe pain. Given parenterally, it is 0.8–0.9 times as potent as morphine[10] and 3–4 times as potent as pentazocine.[11] It is claimed that the dose-related respiratory depression associated with other opioids does not occur with nalbuphine,[12] an effect which would benefit the neonate. Unlike pethidine, whose major metabolite, norpethidine, has depressant effects, nalbuphine is mainly metabolised to an inactive glucuronide conjugate.

The above suggests that it might be a good drug for maternal analgesia. This paper reports a double-blind, between-patient comparison[13] of intramuscular pethidine and nalbuphine for the relief of pain during labour.

Method

Patients selected for the trial had a parity of 4 or less, were more than 38 weeks pregnant with an uncomplicated obstetric history and were healthy. All parturients gave informed consent and the investigation had the approval of the regional ethical committee.

The trial drugs (pethidine 100 mg or nalbuphine 20 mg) dispensed in specially prepared coded ampoules in sets of three were given intramuscularly according to random allocation; each patient received the same drug throughout labour. Repeat medication was only given if an interval of 2 hours had elapsed from the previous dose, with an upper limit of three doses per patient. Any woman who, in the opinion of the investigator, was experiencing inadequate pain relief was withdrawn from the trial and given an epidural block. When a patient requested pain relief during labour, she was asked to grade her discomfort at the peak of a uterine contraction as very severe, severe, moderate or slight and also to record the intensity of her pain on a visual analogue scale. These assessments were repeated at 30, 60 and 90 minutes after each treatment. Maternal blood pressure and heart rate, together with fetal heart rate and any spontaneously mentioned side effects, were noted at these times. These observations, together with the degree of cervical dilatation and the strength, frequency and duration of uterine contractions were recorded on a special chart.

At delivery, maternal and umbilical venous blood samples were drawn for estimation of plasma pethidine and nalbuphine levels. A detailed Apgar minus colour score was recorded for each baby and the reason, if any, for resuscitation was noted. Blood loss at third stage was estimated. A neurobehavioural analysis according to Scanlon *et al.*[14] was carried out at 2–4 hours and at 22–24 hours after delivery by the same clinician. Mothers were interviewed 24 hours after delivery and their subjective evaluation of pain relief and of the efficacy of their therapy was recorded.

Blood samples were collected, heparinised and immediately centrifuged. The plasma was stored at −20°C until analysis. Plasma pethidine concentration was estimated by gas–liquid chromatography using a nitrogen-phosphorus detector with bupivacaine as an internal standard.[15] Plasma nalbuphine concentration was measured by high performance liquid chromatography and electrochemical detection with naloxone as an internal standard.[16] The coefficient of variation of the methods was 4% for pethidine at 500 ng/ml and 4% for nalbuphine at 50 ng/ml.

Results were analysed using the Mann–Whitney U test for nonparametric data and the independent *t*-test for the decremental responses (parametric data).

Results

Of the 80 patients studied, five given pethidine and three given nalbuphine were withdrawn from the investigation because of inadequate pain relief. Table 1 shows that the groups were broadly comparable with regard to their physical and obstetric characteristics.

Six patients in the pethidine group and eight patients in the nalbuphine group required two

Table 1. Physical and obstetric characteristics of patients in the study (mean, SEM)

Treatment	Number of patients	Age (years)	Weight (kg)	Parity			Attended relaxation classes	Mean dilatation of cervix* (cm)	Mode of delivery		Average 3rd stage blood loss (ml)
				1	2	3 or 4			Normal	Forceps	
Pethidine	35	25 (0.9)	72 (1.6)	14	13	8	16	3.3 (0.17)	32	3	206.5
Nalbuphine	37	26 (0.9)	74 (2.0)	13	16	8	10	3.3 (0.18)	36	1	136.7

*At time of first administration of an opiod.

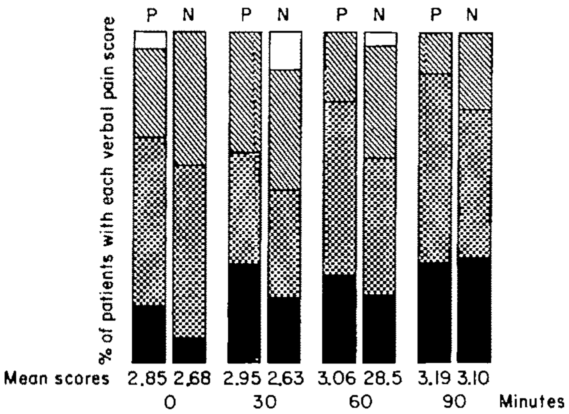

Fig. 1. Histogram of the percentage distribution of verbal pain scores in the first 90 minutes. ☐, Slight; ▨, moderate; ▒, severe; ■, very severe.

Table 2. Numbers of patients reporting pain relief in each group using both methods of assessment of severity

Minutes after drug administration	Visual analogue scale		Verbal pain score	
	P	N	P	N
30	15	18	9	9
60	8	13	3	4
90	4	6	3	2

P, Pethidine; N, nalbuphine.

injections; no patient had three doses. The mean injection–delivery interval of 131 minutes (SEM 10) in the nalbuphine groups differed significantly ($p < 0.001$) from that in the pethidine group, 100 minutes (SEM 9).

Both the average verbal pain scores and the visual analogue scale readings increased throughout labour. At 60 minutes, visual analogue scores ranged from 2–100 (mean 74, SEM 3.5) in the pethidine group and from 8–100 (mean 66, SEM 4.1) in the nalbuphine group. Figure 1 shows the distribution of pain severity in each group with average verbal pain scores at each assessment time. There was no significant difference between the findings in the two groups. With both drugs, the visual analogue indicated better analgesia than the patients' verbal record of its severity (Table 2).

On the day after delivery, the majority of parturients were quite satisfied with their experience of childbirth; 68% of each group were willing to repeat the same treatment in a subsequent labour. However, more detailed questioning with regard to analgesic efficacy revealed that 85% of patients in the pethidine group and 63% in the nalbuphine group felt that their injected treatment had only been minimally effective ($p < 0.05$).

There was less nausea and vomiting after nalbuphine (6) compared with pethidine (14). Eight patients given nalbuphine were considered to be excessively sedated compared with only two in the pethidine group. Dizziness was experienced by seven after pethidine and by twelve after nalbuphine. None of these differences were statistically significant.

The distribution of the infant Apgar minus colour scores (Fig. 2) was similar for each drug. Intramuscular naloxone was required to counteract opioid effects in three neonates, all of whose mothers had received nalbuphine. The total mean neonatal neurobehavioural scores for the 2—4 hours assessment were 25.3 minutes (SEM 0.95) in the pethidine group and 21.6 minutes (SEM 0.81) in the nalbuphine group; this difference was significant ($p < 0.001$). Examination of individual components reveals that the decremental reponse to sound ($p < 0.05$), general body tone ($p < 0.01$) and alertness ($p < 0.05$) accounted for these differences. At 22–24 hours there were no significant differences between the groups; the total mean scores were 31.7 (SEM 0.80) and 32.7 (SEM 0.80) for infants who received pethidine and nalbuphine respectively.

The percentage of individual low neurobehavioural scores (grades 0–1) seen in the two groups are shown in Fig. 3. At 2–4 hours there are always a greater number of depressed scores in the nalbuphine groups than the pethidine group; this difference reached significance in the general assessment ($p < 0.05$). However, at 22–24 hours this situation is reversed in the tests measuring tone, alertness, tone, Moro, rooting and sucking.

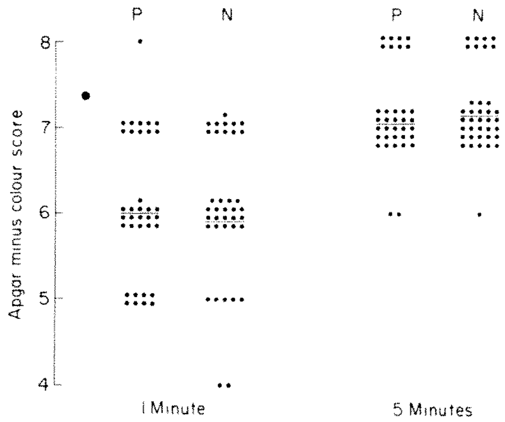

Fig. 2. Apgar minus colour scores at 1 and 5 minutes in the two groups. P, Pethidine; N, nalbuphine.

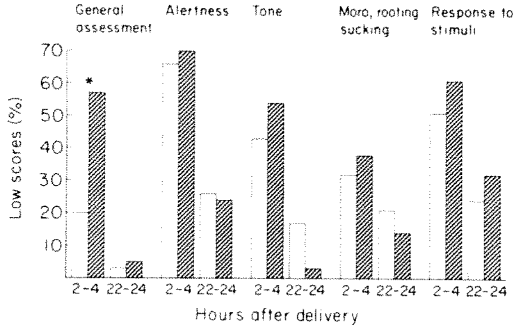

Fig. 3. Percentage of individual low neurobehaviour scores at the assessment times in the two groups. *$p = 0.001$. □, Pethidine; ▨, nalbuphine.

The difference between the mean umbilical vein/maternal vein drug concentration ratio at delivery for nalbuphine 0.78 (SEM 0.03) and for pethidine 0.61 (SEM 0.02) was significant at the 0.01% level. In Fig. 4, in which individual ratios are plotted against the injection–delivery interval, the nalbuphine ratios are consistently higher than those for pethidine, despite the longer injection–delivery interval in this group.

Discussion

According to Melzack[17] the pain of labour ranks second only to that of causalgia in its severity. In addition, it has the unique properties of being intermittent and increasing in intensity over a variable period. These factors combine to make the assessment of analgesic efficacy in labour notoriously difficult.

Judged by both the subjective pain scores and visual analogue scale assessments taken during labour, in the doses used the two drugs were equally effective as analgesics. On retrospective assessment, however, nalbuphine was significantly better than pethidine. This discrepancy between patients' immediate evaluation and later memory may be partly attributable to the tendency to greater sedation in the nalbuphine group. The gradual rise of both verbal pain and visual analogue pain scores throughout the period of labour in the majority of parturients

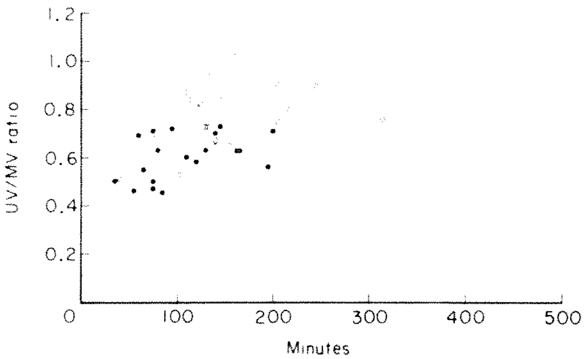

Fig. 4. The umbilical vein/maternal vein plasma drug concentration ratio related to the injection–delivery interval (minutes). ○, Nalbuphine; ●, pethidine.

highlights the inadequacy of intramuscular analgesic treatment for pain relief in labour. Larger doses of opioid might give greater pain relief but would jeopardise infant wellbeing. In this study, only three babies required an opioid antagonist, in each case when maternal nalbuphine had been given and the neonates were excessively sleepy. All recovered within 24–48 hours.

The most notable finding in our study, however, is that in conjunction with a significantly higher mean umbilical vein/maternal vein drug ratio, neonates whose mothers received nalbuphine had consistently lower neurobehavioural responses than in the pethidine treatment group during the 2–4 hours postdelivery period. Transplacental transfer of intravenous nalbuphine has been studied in parturients undergoing elective Caesarean section.[18] The mean umbilical vein/maternal vein ratio found was 1.4 with an injection–delivery interval of 2–10 minutes. The lower mean ratio of 0.78 reported here is probably due to a longer mean injection–delivery interval of 180 minutes and the drug's administration by intramuscular injection. The corresponding mean ratio found for pethidine was 0.61, which suggests that it undergoes less placental transfer than nalbuphine.

On the day after delivery, neonates of mothers given pethidine had a higher percentage of lower neurobehavioural scores with respect to alertness, tone, Moro reflex, rooting and sucking; this suggests that nalbuphine is metabolised by the neonate at a faster rate than pethidine. In addition it is well recognised that the neonatal effects following maternal pethidine last 2–3 days.[9]

It has recently been shown that nalbuphine produced significantly better pain relief following on demand intravenous administration of 3 mg increments than did pethidine in 15 mg increments,[19] while neonatal Apgar and neurobehavioural scores did not differ significantly. Thus it appears that conventional intramuscular administration of opioids may be more hazardous to the neonate.

Moir[20] has advocated that where possible the occurrence of sufficiently severe pain to merit a second dose of pethidine should be an indication for epidural analgesia. This was applied to eight patients in our study and would appear to be the rational policy for a modern labour suite with an epidural service, provided that an advanced stage in labour has not been reached. The total dosage of opioid administered to parturients is correspondingly lower, thus minimising fetal effects.

Early reports[10,21] suggested that nalbuphine was associated with less nausea and vomiting than other opioids. Our findings are broadly in agreement with this claim, but this possible advantage was somewhat offset by a tendency of the drug to produce more maternal sedation and dizziness and more early neonatal neurobehavioural depression than pethidine.

This study confirms that labour pain is ineffectively treated with intramuscular opioids, but, paradoxically, finds that the majority of women are happy to have similar pain relief for subsequent labours, demonstrating perhaps that this technique remains popular. On the basis of this study, nalbuphine would not appear to offer a substantial improvement over pethidine for pain relief in labour.

Acknowledgments

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Anaesthesia, 1986, Volume 41, pages 1214–1218

CASE REPORT

Respiratory disturbance and posterior fossa surgery

A case report

A. P. YATES, E. SUMNER AND S. G. E. LINDAHL

Summary

This report, of a 16-month-old child recovering from surgery for a posterior fossa tumour, illustrates how pneumotachography, capnography and occlusion testing before and during CO_2 *challenge can be of clinical value in the analysis of a difficult respiratory disturbance in the early postoperative period. The application of these techniques to assist decisions regarding timing of extubation as well as for assessment of the influence of remaining tumour on respiratory competence is discussed.*

Key words

Complications; postoperative.
Surgery; neurological, posterior fossa.

Postoperative controlled ventilation may be indicated after neurosurgical procedures to control the problems of postoperative cerebral oedema. This is particularly important after posterior fossa surgery involving manipulation of the brain stem. In this report, the occurrence of prolonged postoperative ventilatory disturbance after posterior fossa surgery in a 16-month-old child is reported. The respiratory pattern, the ventilatory CO_2 response together with intra-airway pressure at occlusion, were evaluated before tracheal extubation.

Case history

The patient, a 16-month-old male, presented with failure to thrive and a 3-month history of choking and vomiting unrelated to feeding or time of day. Examination revealed a normal but malnourished child weighing 7.9 kg with intact cranial and peripheral nerves and no evidence of cardiorespiratory abnormality. A computerised tomographic (CT) head scan revealed a space-occupying lesion in the region of the lower vermis, which was compressing the lower part of the fourth ventricle, but with no evidence of hydrocephalus. A diagnosis of a fourth ventricular tumour was made and the patient underwent a posterior fossa craniotomy and exploration in the sitting position.

Premedication consisted of atropine 0.2 mg with dexamethasone 2 mg given intravenously at anaesthetic induction. The patient was ventilated throughout and given incremental tubocurarine, fentanyl and halothane 0–0.5% to maintain

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anaesthesia whilst intra-arterial blood pressure and end-tidal CO_2 levels were recorded continuously. The tumour was found to arise from the floor of the fourth ventricle and extended downwards into the spinal canal and upwards to emerge between the cerebellar tonsils. Complete removal was not possible and tumour was left on the lower half of the floor of the fourth ventricle. Dissection in this region was associated with profound fluctuations in heart rate and blood pressure which were controlled with labetalol; surgical haemostasis was then secured (although total blood loss was considered to be minimal) and the wound closed.

Elective postoperative ventilation for 24 hours was undertaken in view of the cardiovascular instability; over this period of time the heart rate and blood pressure remained extremely labile, despite adequate sedation, and required further administration of labetalol. Dexamethasone 2 mg was continued 6-hourly. The following morning with chest X ray and blood gas analysis within normal limits, the patient who was awake and responsive underwent a trial of spontaneous ventilation. It was difficult to assess the respiratory rhythm because he appeared overtly distressed and agitated, but it was thought that the tidal breaths were clinically adequate and he was extubated shortly after. However, although he was able to maintain an adequate airway he suffered from recurrent apnoeic attacks, with cyanosis and bradycardia, and required stimulation to initiate breathing. The decision was taken to re-intubate and ventilate the patient for a further 24 hours, by which time it was considered that there should be no possibility of residual drug-induced central depression. During spontaneous respiration whilst intubated, it became apparent that the patient's respiratory rhythm was irregular and unpredictable, but it was not possible to assess whether or not this was related to the presence of the tracheal tube. He thus underwent a trial of extubation. Further apnoeic and cyanotic periods ensued and the patient was again re-intubated, but allowed to breathe spontaneously with continuous positive airway pressure (CPAP) of 0.5 kPa. Under these conditions his respiratory rhythm remained irregular but there were no further episodes of cyanosis or bradycardia. A repeat CT scan at this time showed no evidence of blood or fluid collection in the region of the fourth ventricle and no hydrocephalus or midbrain distortion.

Measurements

A pneumotachograph (Fleisch No 0), an in-line capnograph (Hewlett–Packard 14360 A) and connexions for an airway occluder were placed in the circuit deadspace (Fig. 1). Airway pressure was measured at the tube connexion by a pressure transducer (Druck PDCR-75) and ventilation volume by electrical integration of the flow signal from the pneumotachograph and a differential pressure transducer (Validyne MP 45-1-871, range ±0.2 kPa). Signals for flow, volume, pressure and CO_2 were recorded on an ink-jet recorder (Siemens Elema EM 81). The airway occlusion occurred precisely when expiration switched to inspiration, i.e. at the functional residual capacity (FRC). Recordings of flow, volume, CO_2 and intra-airway occlusion pressure (P^o) were performed during quiet breathing. Then inhalation of 4% CO_2 (from a gas cylinder) was started and continued for 10 minutes, after which time the measurements were repeated.

Results

After 6 hours of breathing spontaneously with CPAP the first set of recordings were taken when the patient was asleep. His breathing was irregular, with a slow respiratory rate (14–16 breaths/minute) and periods of apnoea (which were reported to be less frequent than when he was awake). Lung function studies revealed a variable respiratory pattern during sleep, with tidal volumes varying between 57 ml (7.2 ml/kg) and 107 ml (13.5 ml/kg; Fig. 2). During periods of low tidal volume, end-tidal CO_2 tensions ($P_{E'CO_2}$) increased but varied only within 0.5 kPa. When he awoke, tidal volumes were generally greater and $P_{E'CO_2}$ tensions lower, but periods of apnoea lasting up to 16 seconds were noted which started after exhalation (Fig. 2).

Respiratory stimulation with 4% CO_2 added to the inspired gas was recorded in the awake state and a more regular pattern of breathing was noted with a compensatory increase in tidal volume and respiratory rate, so that $P_{E'CO_2}$ tensions were only moderately increased (Fig. 3). The maximal intra-airway pressure during airway occlusion (P^o_{max}) was −1.6 kPa before and −2.9 kPa during CO_2-stimulated breathing (Fig. 3).

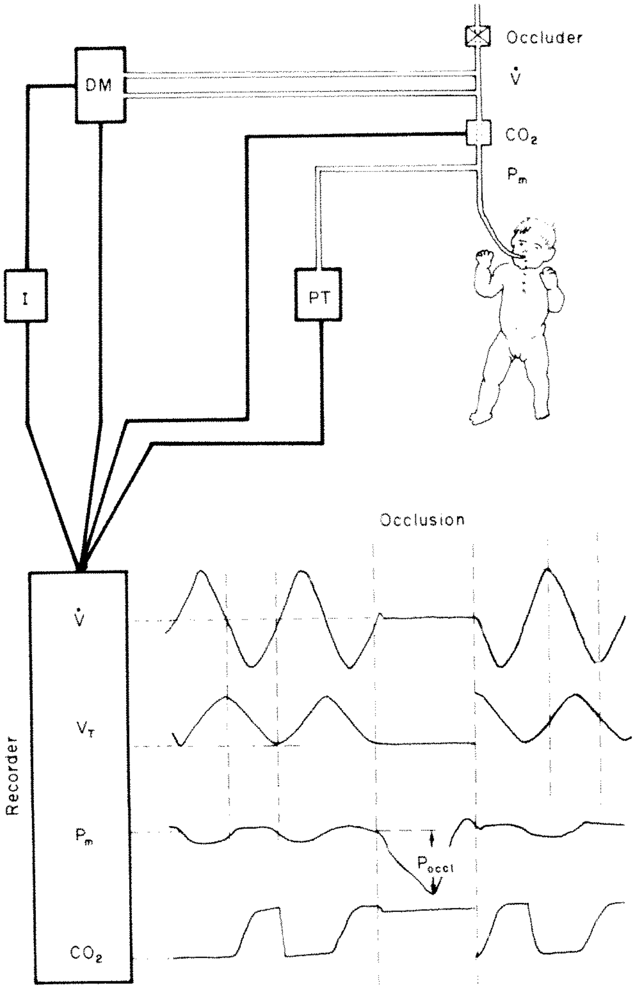

Fig. 1. Schematic representation of the set up and of recorded variables. $\dot{V}$ indicates flow, CO_2 indicates position of the in-line capnograph and P_m the place for airway pressure measurements.

Discussion

The continued presence of tumour in this child, together with the postoperative inflammatory reaction, most probably accounted for the prolonged brainstem dysfunction. It was, however, difficult to interpret his respiratory pattern during weaning because of the tendency to become agitated and distressed when not sedated. Although the number of apnoeic periods was not quantified, either in the awake or asleep state, it was clinically apparent that these episodes were more severe (and at times life threatening) when the patient was awake and extubated than whilst he was intubated. It is possible that the continual stimulation due to the presence of the tracheal tube promoted an increased respiratory centre output. To further elucidate his respiratory disturbance, bedside measurements of ventilation, CO_2 response and respiratory drive were therefore performed while he remained intubated.

When asleep 2 days after the operation he had periodic spontaneous breathing of a kind similar to the Cheyne-Stokes pattern, whilst managing to maintain his end-tidal CO_2 tension within

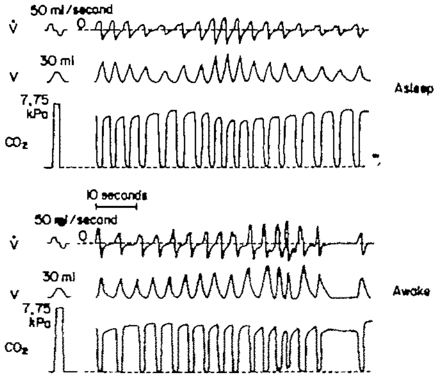

Fig. 2. Recordings of respiratory flow ($\dot{V}$, inspiration upwards), tidal volume (V) and CO_2 tension (CO_2) in the asleep as well as in the awake state. Note the periodic respiratory pattern during sleep and the apnoeic spell of almost 10 seconds when awake.

acceptable limits. In the awake state the periodicity was less well marked and end-tidal CO_2 tensions were lower than when asleep. On the other hand, he had frequent apnoeic spells of up to 16 seconds duration. The apnoea always occurred at functional residual capacity (at the end of a completed exhalation), which suggests that the output from neurones responsible for the on-switch mechanism was inadequate. Inspiration after a period of apnoea was vigorous and this ability to increase tidal volume intermittently and during CO_2 stimulation suggested that the peripheral neuromuscular components of diaphragmatic function were intact. In a study by Scott and co-workers[1] of near-miss sudden death infants they found that diaphragm function was normal or improved in those patients, i.e. diaphragmatic competence was preserved.

The delayed inspiratory switch-on mechanism was dependent upon the CO_2 tension, since at a 4% CO_2 stimulation the respiratory pattern became regular and no apnoeic spells were recorded during the 8 minutes of CO_2 breathing. The respiratory rate was also faster during CO_2 breathing which, together with the larger tidal volumes, demonstrated a normal CO_2 response in awake patients.[2] This indicated that the bulbopontine pacemaker function was reactive to CO_2 and suggested that this was the case also for the respiratory centre. The intra-airway pressure during airway occlusion in this child (occlusion pressure is proportional to the phrenic nerve discharge[3]) was, however, only −1.6 kPa in the awake state, which is low compared with normal children breathing spontaneously under halothane anaesthesia (unpublished observations). Perhaps most importantly, they showed a flat pressure curve immediately after the occlusion, suggesting that the neuronal output of the intended breath (which is reflected during early occlusion[3]) was reduced. However, during CO_2 breathing this was improved in that a fast steep pressure curve of the early occluded phase was recorded and the maximal occluded intra-airway pressure was more pronounced: −2.9 kPa compared with −1.6 kPa before CO_2 stimulation (Fig. 3). This also supports the contention that CO_2 breathing not only improved the bulbopontine pacemaker function in this child, but also the respiratory drive by promoting an increased centre output.

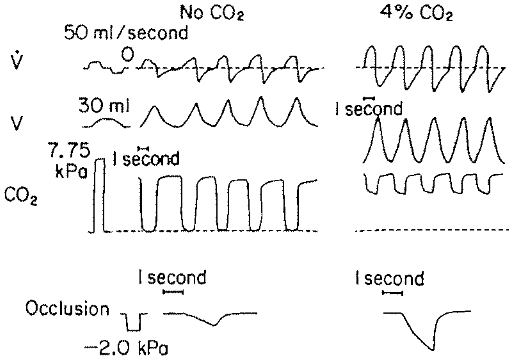

Fig. 3. Recordings of respiratory flow ($\dot{V}$, inspiration upwards), tidal volume (V), exhaled and inhaled CO_2 tension (CO_2) and intra-airway occlusion pressures (Occlusion) before and during CO_2 breathing. Note the faster and more regular breathing during CO_2 stimulation and the change in early phases of occlusion before and during CO_2 breathing.

Successful extubation of this child was encouraged because of these measurements, as the respiratory rhythm centre and the respiratory motor centre were both shown to be reactive. However, these measurements also demonstrated that respiratory function was disturbed, justifying very close observation after extubation and; perhaps more importantly, that the respiratory disturbance was probably a symptom arising from the remains of the fourth ventricular tumour.

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Anaesthesia, 1986, Volume 41, pages 1219–1224

CASE REPORT

Pompe's disease and anaesthesia

H.J. McFARLANE AND N. SONI

Summary

A case report of a child with Pompe's disease (glycogen storage disease Cori type II), who underwent two general anaesthetics, is presented. The progressive infiltration of heart and skeletal muscle with glycogen results in a severe form of cardiomyopathy and respiratory muscle weakness. Consequently, there are significant problems in the anaesthetic management of these patients. Although there are theoretical attractions for some anaesthetic drugs, the key factors in a successful outcome are attention to anaesthetic technique and close monitoring.

Key words

Anaesthesia; Pompe's disease.

Pompe's disease is a rare defect of glycogen metabolism with an autosomal recessive pattern of transmission. It is associated with generalised deposition of glycogen throughout the body, but affects principally the heart and skeletal muscle. The condition is due to the absence of acid α glucosidase, a glycogen-degrading enzyme normally present in lysosomes, and is classified as a Cori type II glycogenosis. Other glycogen storage diseases are associated with defects in enzymes situated within the cytoplasm. In Pompe's disease these enzymes are normal and hence blood sugar and glucose tolerance tests are within normal limits.[1]

A baby born with Pompe's disease may appear clinically normal at birth, but after a few weeks becomes floppy and commonly presents with feeding difficulties. The liver may enlarge, but the massive hepatomegaly associated with Von Gierke's disease is not seen. The ECG shows features of biventricular hypertrophy with a characteristic short PR interval,[2] and chest X ray confirms the presence of cardiomegaly. Atelectasis may occur due to compression of bronchi by the enlarged heart; this results in respiratory distress often associated with open mouth breathing and protrusion of the tongue. These appearances of air hunger may mimic macroglossia, although true macroglossia can also be present. The disease process is rapidly progressive and few children survive beyond one year. The usual cause of death is respiratory failure due to muscle weakness, often complicated by aspiration pneumonia or progressive cardiac failure. Sudden death can occur as a result of obstructive myopathy involving the outflow tract of one or both ventricles. The diagnosis is made on clinical grounds, by enzyme studies and by the demonstration of massive glycogen deposition in lymphocytes in peripheral blood.

There is a milder form of the disease, Cori type II B, which first presents in the third or fourth

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decade with muscle weakness simulating dystrophy. Life span can be normal, although the level of activity is markedly impaired. Cardiomegaly is absent and the ECG is normal. This form does not occur in the same families as Pompe's disease and is a genetic abnormality probably associated with a reduced amount of lysosomal α glucosidase.

At present there is no known cure for Pompe's disease and symptomatic treatment does not prolong survival beyond 18 months. As these children are mentally normal, bone marrow transplantation is now being offered as a potential cure. It is inevitable, therefore, that anaesthetists will become involved to provide suitable conditions for marrow aspiration, tissue biopsies and the insertion of central lines. It is for this reason that we present our experiences with one child suffering from the disease, who underwent two general anaesthetics.

Case history

The patient, a female child of 5 months, was the fourth child born to Asian parents. She had two sisters aged 6½ and 3 years who were alive and well and one brother who had died at 6 months from Pompe's disease. At birth she was well but noted to be floppy and in view of the family history she was investigated and Pompe's disease was confirmed. At 3 months she presented with feeding difficulties and episodes of cyanosis during feeding. Signs of cardiac failure were present, which responded to diuretic therapy. At this stage bone marrow transplant was considered and the youngest sibling was found to be a suitable donor. A few weeks later she was presented for insertion of a Hickman line, marrow aspiration, liver biopsy and muscle biopsy. Preoperatively she weighed 4.9 kg, cardiac failure was controlled with frusemide 12 mg daily and ECG showed biventricular hypertrophy with characteristic short PR interval. Chest X ray showed an enormous heart with left lower lobe collapse (Fig. 1). Echocardiography showed generalised hypertrophy of the myocardium, especially the left ventricle and interventricular septum, with slight dilatation of the left ventricular cavity. The left ventricle was seen to be contracting poorly but, in view of the diagnosis, the echo was described as showing moderate disease only.

First anaesthetic

Premedication consisted of atropine 0.1 mg intramuscularly. On arrival in the anaesthetic room, intravenous access was established and a variety of resuscitative drugs made ready. It was planned to institute ECG monitoring on loss of consciousness and, following pre-oxygenation, anaesthesia was induced with oxygen, nitrous oxide and increasing concentrations of halothane. About 30 seconds after the start of induction, heart rate decreased to 80 beats/minute from a pre-induction level of 120. This responded to atropine 0.12 mg intravenously. Two minutes later, with the inhaled concentration of halothane at 2%, further bradycardia ensued. The child looked pale, and it was decided to intubate the trachea without delay. Further atropine 0.12 mg was given, followed by suxamethonium 10 mg. Following inflation of the lungs with oxygen, intubation was carried out without problem. At this stage the child was found to be pulseless and external cardiac massage was instituted.

While awaiting the attachment of ECG electrodes, adrenaline 10 μg and sodium bicarbonate 5 mmol were given. The ECG showed ventricular fibrillation and three direct current shocks were required to convert this to complete heart block. Isoprenaline 10 μg and atropine 0.12 mg increased the heart rate and at this stage a clinically satisfactory circulation was re-established. Because of the presence of tall, peaked T-waves on the ECG, calcium chloride 1 mmol was given. After 5 minutes the heart rhythm had stabilised, colour was good, the child was breathing spontaneously and moving all four limbs normally; pupillary responses were also normal. It was decided to abandon the procedure, extubate the trachea, and transfer the child to the intensive care unit. Postoperatively she remained well, apart from the new feature of a loud pansystolic murmur. Slight arterial desaturation responded to an increase in the fractional inspired oxygen concentration to 0.3. A repeat echocardiogram showed increase in left ventricular hypertrophy, with a smaller left ventricular cavity and trivial mitral regurgitation. Over the course of the next 2 or 3 days the murmur disappeared. One week later the child was again presented for consideration of anaesthesia. Her cardiac status was stable, but she had persistent left lower lobe collapse. Following prolonged dis-

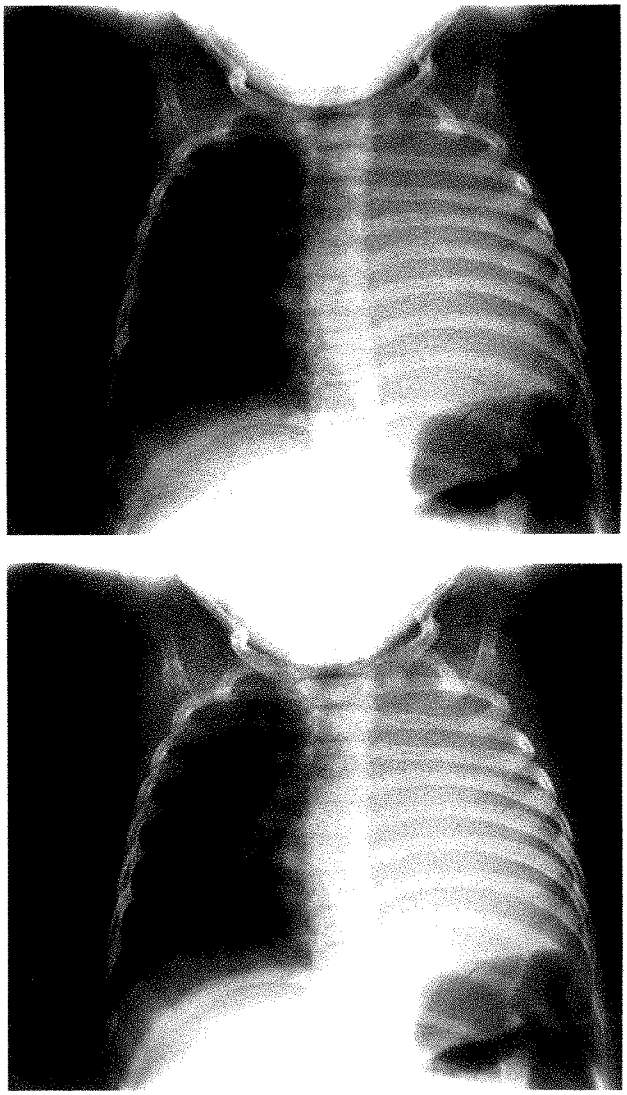

Fig. 1. Pre-operative chest X ray showing left lower lobe collapse and massive cardiomegaly.

cussion with the parents, and in view of the hopeless prognosis without treatment, it was decided to proceed with further anaesthesia.

Second anaesthetic

Premedication again consisted of atropine 0.1 intramuscularly and, at the same time, an intravenous infusion of 10% dextrose was started to run at a maintenance level according to her weight. In theatre, ECG electrodes were applied and, following 3 mg of ketamine intravenously a left femoral arterial catheter was inserted and connected to a pressure monitor. Following preoxygenation, a further 10 mg ketamine was given intravenously with 0.5 mg vecuronium, and the lungs ventilated via a facemask. The heart rate dropped to 100 beats/minute, but this was restored to the pre-induction level of 140 with atropine 0.12 mg. Following tracheal intubation, the lungs were ventilated with a 50:50 mixture of oxygen and nitrous oxide using the Jackson-Rees modification of the Ayre's T-piece. Surgery commenced and during the procedure, which lasted 65 minutes, the child received a further 3 mg of ketamine in divided doses and a further 0.2 mg vecuronium in response to movement occurring 40 minutes after the start of induction. Heart rate and blood pressure remained stable. At the end of surgery bronchoscopy was performed and some thick secretion was aspirated from the left main bronchus. Neuromuscular blockade was reversed with atropine 0.15 mg and neostigmine 0.3 mg 40 minutes after the last dose of vecuronium and the trachea was extubated uneventfully. Postoperatively she remained well, but with a productive cough which required physiotherapy.

Discussion

Previous anaesthetic experience of this condition is sparse, due to the short life expectancy and rarity of the condition. Kaplan[3] reported two cases who underwent a variety of procedures at different stages of the disease and who were exposed to a variety of anaesthetic agents including halothane, nitrous oxide, ether, suxamethonium and ketamine. From his experience with the second child he suggests that, although the children have hypotonia and may appear weak, their anaesthetic requirements are not lessened. Ellis[4] describes a cardiac arrest occurring in a child during halothane induction, where the diagnosis of Pompe's disease was made post mortem.

There are three main problems facing the anaesthetist in this condition.

The cardiomyopathy

The massive infiltration of the ventricular wall in Pompe's disease may produce either a congestive or obstructive cardiomyopathy. In the former, the management would be as for congestive cardiac failure. This includes avoidance of myocardial depression during induction and pharmacological manipulation of the circulation to reduce preload, increase myocardial contractility and reduce afterload. In the obstructive type of myopathy, anaesthetic agents such as ketamine, or support agents with chronotropic or inotropic action, are relatively contraindicated because they may increase the degree of obstruction.[5] There appear to be wide differences of opinion as to the agent of choice in the obstructive type myopathy. Halothane may be contraindicated,[6] because of the potential for the development of a malignant dysrhythmia, or indicated[5] because of the reduction in contractility and slow heart rate, features which tend to minimise the obstruction. In this particular child, the echo suggested that the main problem was obstruction to ventricular filling rather than emptying.

While these theoretical arguments are of interest, the disease process in Pompe's is such that if obstruction is present due to massive accumulation of glycogen, there is inability to increase either ventricular muscle mass or contractility in response to the obstruction.[5] The safest course of action would be to utilise agents with which one is most familiar and to monitor closely, and react quickly to, changes in cardiovascular status. We consider that the difference in outcome between the first and second anaesthetic was due to the close monitoring, rather than to the agents employed. The most likely cause of bradycardia occurring during the early phase of both inductions was hypoxia, especially in view of the pre-operative chest X ray.

Oxygenation

Classically, children with Pompe's disease are described as having large tongues, but a tendency to protrude the tongue and hence give the appearance of macroglossia may be a feature of air hunger. If macroglossia is present, then awake intubation following glycopyrronium has been recommended.[7] In the presence of hypotonia this may be feasible, but with this child hypotonia was not a prominent feature and the tongue size was normal. Awake intubation in a child of 5 months could have been unnecessarily traumatic. In the first case described by Kaplan,[3] a large tongue could have been responsible for loss of airway control during anaesthesia. Whether or not the tongue is large, oxygenation may be severely compromised by any loss of airway control during induction.

The large heart may compress major bronchi and result in collapse. Intercurrent infection should be treated by appropriate antibiotics and physiotherapy, but re-inflation of a collapsed lobe may prove very difficult. The major shunt thus created means that oxygenation is critical and high inspired oxygen concentrations should be used from the outset during induction.

Respiratory muscle weakness and the use of muscle relaxants

Muscle weakness occurs within weeks of birth and is progressive, due to increasing glycogen deposition. Muscle damage may occur due to the release of lysosomal contents following rupture of the glycogen-containing sacs. In this patient, electron microscopy confirmed the destruction and attenuation of muscle fibres. Respiratory failure is the commonest terminal event and may be provoked by lobar collapse or aspiration pneumonia. Marked hypotonia pre-operatively may obviate the need for neuromuscular blockade, but may lead to problems with ventilation postoperatively. Elective postoperative ventilation may be required to allow the effects of depressant drugs to wear off, but there is always the danger with advanced disease of never establishing adequate ventilation postoperatively without assistance. In less advanced disease, neuromuscular blockade may be required to facilitate intubation at a relatively light plane of anaesthesia.

There are, intuitively, drawbacks to the use of suxamethonium in a patient with myopathy. Firstly, there is the problem of potassium efflux following suxamethonium. If muscle damage has occurred as a result of lysosomal rupture, then the muscle could have increased chemosensitivity. Even minor muscle damage can increase chemosensitivity and hence the potential for increased potassium efflux following suxamethonium.[8] The serum potassium before the first anaesthetic was 3.5 mmol/litre and, following the arrest, was 3.7 mmol/litre. However, about 20 minutes had elapsed between suxamethonium administration and the sample and an acute rise in serum potassium cannot therefore be excluded. The peaked T-waves after restoration of sinus rhythm, suggesting hyperkalaemia, may have been due to acidosis. Secondly, there is the problem of suxamethonium and the development of malignant hyperthermia syndrome or myoglobinuria. There is one case report in the literature of hyperpyrexia assoicated with anaesthesia in glycogen storage disease.[9] Ellis and Heffron[10] comments on this case by pointing out that, firstly, the associated ketoacidosis probably indicates a different metabolic aetiology and, secondly, that muscle susceptible to malignant hyperthermia is deficient in glycogen, which is the converse of that in glycogen storage disease.

Myoglobinuria can occur in association with McArdle's disease (Type V) and, as pointed out by Coleman,[11] suxamethonium should be avoided lest it precipitate myoglobinuria, with the risk of renal failure. Both these case reports refer to patients with different types of glycogenosis, exhibiting different biochemical pathological and clinical entities. However, as Ellis and Heffron[10] suggest, any patient with muscle disease should have his body temperature monitored under anaesthesia and suxamethonium should be avoided due to the danger of rhabdomyolysis.

If neuromuscular blockade is required, either to facilitate intubation or to maintain anaesthesia at a relatively light plane, then the relaxant of choice would be one with minimal cardiovascular effect and short duration of action. In view of the cardiovascular stability, we opted for vecuronium in the second anaesthetic. Glycogen deposition in the liver is not a feature of Pompe's disease and, since there was no evidence of right heart failure with hepatic congestion, we felt that the metabolism of vecuronium would not be prolonged. No monitoring of neuromuscular function was utilised, but movement occurred 40 minutes after a dose of 0.1 mg/kg. In the absence of a volatile agent this would be considered a long duration of action, but it was not a problem in this case. If hepatic function is compromised, atracurium would be the relaxant of choice, as it undergoes spontaneous degradation at physiological pH and body temperature.

If marrow transplantation can offer survival to children with Pompe's disease, then it is likely that these children will be presented for anaesthesia more commonly in future. Provided the disease process is not too far advanced, the respiratory and cardiac problems can be overcome by attention to anaesthetic technique and close monitoring, rather than by the choice of specific anaesthetic drugs. Suxamethonium should be avoided because of the risk of rhabdomyolysis. The need for neuromuscular blockade can be assessed by the degree of hypotonia pre-operatively and, if sufficient tone is present, neuromuscular blockade should be employed to gain early control of the airway, thus ensuring oxygenation and avoiding the potentially harmful myocardial effects of deep anaesthesia.

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CASE REPORT

Vecuronium and phaeochromocytoma

A report of two cases using different modes of administration

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Summary

Two patients presenting for removal of phaeochromocytoma are described. Vecuronium was used to provide neuromuscular blockade by two different methods of administration: an infusion and a large bolus dose. Both gave satisfactory results and we suggest that vecuronium may be the neuromuscular blocking agent of choice for patients with phaeochromocytoma.

Key words

Neuromuscular relaxants; vecuronium.
Surgery; phaeochromocytoma.

Vecuronium has been shown to be remarkably cardiostable[1–4] and to cause minimal histamine release.[5] These properties suggest that it may be the muscle relaxant of choice for patients with phaeochromocytoma.[6] We report the details of two patients in whom vecuronium was administered by different modes in order to achieve muscle relaxation during anaesthesia for phaeochromocytoma removal.

Case histories

Case 1

A 37-year-old male weighing 69 kg presented for removal of phaeochromocytoma. He had a 2-year history of hypertension which had been diagnosed during an admission to hospital for a nasal operation. He had a hypertensive reaction and marked cardiac dysrhythmias during anaesthesia on that occasion. The acute episode was treated with intravenous practolol and he was discharged to the care of his general practitioner who treated his hypertension with a β-adrenergic antagonist which was later changed to spironolactone.

Earlier in the year he presented again for minor surgery to a toe. His arterial blood pressure was 180/120 mmHg. He was premedicated with papaveretum 15 mg and hyoscine 0.3 mg one hour pre-operatively and was noted to be anxious on arrival in the anaesthetic room. Anaesthesia was induced with thiopentone; he then developed severe hypertension (systolic arterial pressure 200 mmHg) and a tachycardia of 140 beats/minute. This eventually responded to an infusion of sodium nitroprusside and a bolus of practolol. A preliminary diagnosis of phaeochromocytoma

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was made and this was confirmed following estimation of urinary catecholamine metabolites. He was started on labetolol 100 mg twice daily. A postoperative ECG showed ST elevation and T-wave inversion in leads V_{2-4}.

He was transferred to this hospital for definitive treatment. He gave a 2-year history of episodes of palpitations, sweating, headaches and anxiety attacks, which occurred 1–2 times a month and were often brought on by straining at stool.

Physical examination was normal, apart from an arterial blood pressure of 170/100 mmHg. Serum and urinary catecholamine levels were markedly raised. A random blood sugar was 6.3 mmol/litre (normal range 3.3–5.5 mmol/litre). Other blood results were normal. The ECG showed evidence of a small anteroseptal infarct with subendocardial extension. This had most probably occurred during his last anaesthetic. Computerised tomography and an I^{131}-labelled meta-iodo-benzyl-guanidine (MIBG)[7] scan showed a solitary phaeochromocytoma in the region of the left adrenal.

Adequate control of his blood pressure was achieved following 40 days incremental treatment with phenoxybenzamine 90 mg tds, propranolol 60 mg tds and α-methyl-para-tyrosine[8] 500 mg three times a day. When his arterial blood pressure had fallen to 120/80–130/90 mmHg, he was prepared for surgery. He was alert and complained of feeling restless and agitated.

He was premedicated with papaveretum 20 mg and hyoscine 0.4 mg one hour pre-operatively and arrived in the anaesthetic room very sedated. ECG leads and an automatic blood pressure cuff (Accutor Datascope) were placed and baseline readings obtained. Anaesthesia was induced with nitrous oxide in 30% oxygen and isoflurane up to 2%. An intravenous line and a radial artery cannula were sited and a continuous display of arterial blood pressure obtained. Electrodes for the neuromuscular transmission monitor (Datex Relaxograph) were placed over the left ulnar nerve and hypothenar eminence and calibration and baseline values were obtained. Fentanyl 1.5 μg/kg and vecuronium 28 mg (0.4 mg/kg, ED_{95} × 8) were given into a fast-running infusion. Neuromuscular blockade was monitored by train-of-four (TOF) stimulation every 20 seconds.

Ventilation of the lungs was assisted at the onset of paralysis, laryngoscopy performed and the larynx sprayed with 4% lignocaine. The trachea was intubated within 90 seconds of administration of the vecuronium. There was no increase in either heart rate or arterial blood pressure in response to either relaxant administration, laryngoscopy or tracheal intubation. A central venous catheter was sited via the right internal jugular vein and the bladder was catheterised. Anaesthesia was maintained with nitrous oxide in 30% oxygen with isoflurane 0.5–1%. The patient was gently turned to the right lateral position and surgery allowed to proceed. Neither position nor surgical incision produced responses in either heart rate or arterial blood pressure.

Dissection and manipulation of the tumour initiated a rise in arterial blood pressure to a peak of 182/117 mmHg which was treated first by increasing the isoflurane concentration to 2%, then by increments of phentolamine 1 mg to a total of 7 mg and finally by a brief infusion of sodium nitroprusside. The arterial blood pressure settled to a systolic of 100 mmHg over a period of 15 minutes. No dysrhythmias were seen. The arterial blood pressure decreased rapidly to 80 mmHg systolic after removal of the tumour and 2 mg methoxamine were administered to return it to 100 mmHg. Blood loss was 350 ml. The remainder of the operative course was uneventful and no further increments of analgesia or muscle relaxant were required.

T_1 had returned to 20% of control at the end of the procedure, one hour and 55 minutes after the injection of vecuronium. Neuromuscular blockade was reversed with edrophonium 0.5 mg/kg and glycopyrrolate 0.005 mg/kg. Reversal was prompt with a return of T_1 to 50% of control and a T_4 ratio of 0.5 within a minute. The isoflurane was switched off and the trachea extubated once spontaneous ventilation was established.

The patient remained very drowsy in the postoperative period, and was still not fully awake some 12 hours postoperatively, despite a normal blood sugar level.[9] Large volumes of colloid were required to maintain central venous pressure, arterial blood pressure and urine output in the first 24 hours and the patient required 3 litres of plasma and 2 units of blood. He developed a staphylococcal pneumonia within the first 14 postoperative hours for which he required controlled ventilation of the lungs for 30 hours. He responded well to physiotherapy and a course of cephazolin and his further postoperative course was uneventful.

Case 2

A 30-year-old female presented for removal of phaeochromocytoma. She was discovered to be hypertensive earlier in the year, when she visited her general practitioner to be prescribed the oral contraceptive pill. Her only complaint was of occasional episodes of palpitations and in the course of investigation she was found to have raised levels of vanillylmandelic acid. She had had uneventful general anaesthesia in both 1980 and 1983 and was noted to be normotensive on both occasions. Her general practitioner had started treating her with nifedipine slow release 20 mg twice daily.

On admission, her arterial blood pressure was 220/120 mmHg. Her physical examination was otherwise normal. She gave a one-year history of attacks of palpitations. She was taking no medication apart from nifedipine. She had raised urinary and serum catecholamine levels and mildly raised thyroid function tests. An I^{131} MIBG scan showed an area of massive uptake above the left kidney. Her ECG showed sinus tachycardia.

Her blood pressure after admission stabilised at 110/70 mmHg after 3 weeks treatment with phenoxybenzamine 30 mg, propranolol 20 mg and nifedipine 20 mg all twice daily and Lugol's iodine (10 drops/day) for six days.

She was premedicated with lorazepam 2 mg orally 2 hours pre-operatively, followed by papaveretum 15 mg and hyoscine 0.3 mg an hour later. On arrival in the anaesthetic room fentanyl 100 μg was given by slow intravenous injection through an indwelling needle. A radial artery cannula, an intravenous cannula and a right atrial cannula via the right internal jugular vein were all sited under local anaesthesia. Electrodes for the neuromuscular transmission monitor (Datex Relaxograph) were placed as described previously. Anaesthesia was induced with thiopentone 250 mg followed by a further 150 μg fentanyl. Ventilation was assisted by facemask, while calibration and baseline recordings of neuromuscular function were obtained. Vecuronium 5 mg was administered and, after an interval of 2 minutes, the trachea was intubated. There was no rise in heart rate or blood pressure following either induction of anaesthesia, relaxant administration or intubation of the trachea. Anaesthesia was maintained with nitrous oxide in 33% oxygen and isoflurane 0.5–1%. Ventilation of the lungs was controlled to maintain normocarbia (Datex capnograph). Neuromuscular function was monitored by train-of-four every 20 seconds. When twitch height had returned to 10% of control an infusion of vecuronium (0.2 mg/ml) was started.[10] The infusion was delivered by a Vickers Treonic syringe pump and adjusted to maintain a twitch height between 10% and 15% of control.

Surgical incision and abdominal exploration produced a rise in blood pressure to a peak of 200 mmHg systolic. This was treated with increments of phentolamine 1 mg (total 5 mg). Blood pressure settled to control within minutes of removal of the tumour. There were no dysrhythmias. Blood loss was approximately 500 ml.

The vecuronium infusion was stopped towards the end of the procedure and at the end of surgery T_1 had reached 50% of control. Residual neuromuscular blockade was reversed with neostigmine 2.5 mg and glycopyrrolate 0.5 mg. A T_4 ratio of 0.5 was achieved within a minute of reversal. Anaesthesia had lasted for 90 minutes and 1.8 mg of the vecuronium infusion had been administered. When spontaneous ventilation was established, the trachea was extubated and the patient transferred to the intensive care unit where she made an uneventful recovery.

Discussion

The mortality due to surgery for removal of phaeochromocytoma has declined dramatically over the past three decades.[11–13] A number of factors have probably contributed to this decline,[13,14] although the precise role of improved anaesthetic technique is difficult to quantify.[15] There is, however, no doubt that the choice of anaesthetic agent(s) can, and does, influence the incidence of intra-operative complications such as hypertension and dysrhythmia.[14,16]

All muscle relaxants, with the possible exception of vecuronium, have the potential to cause cardiovascular side effects which may, or may not, be associated with histamine release. In patients with phaeochromocytoma, histamine release is particularly undesirable because it can cause hypertension and indeed, this has been used as a diagnostic test for the condition.[17] Vecuronium probably has the least tendency to cause histamine release[3,18] of all the available relaxants. Suxamethonium is relatively contraindicated in patients with phaeochromocytoma, both because of its autonomic side effects[19–21] and also because fasciculations may cause release of catecholamines from the tumour.[16] Pancuronium has little potential to initiate histamine release,[3] but it has been reported to cause hypertension in a patient with phaeochromocytoma,[22] presumably due to its sympathomimetic activity.[23,24] Similarly, gallamine has sympathetic activity which, coupled with a marked tachycardia due to vagal blockade, means this agent is unsuitable.[14]

Theoretically, therefore, vecuronium appears to be the agent of choice for patients with phaeochromocytoma and its successful use in this situation has been reported.[6] The customary method of administration by intermittent bolus doses has the disadvantage that it results in fluctuating levels of muscle relaxation. This may be particularly undesirable in patients with phaeochromocytoma, in whom coughing and straining may cause sudden massive catecholamine release.[25]

Administration by infusion has been suggested as an answer to this problem and in our report this technique worked satisfactorily. However, the use of infusions of muscle relaxant necessitates the availability of a method of reliable delivery of the drug and of monitors of effect; without these, the technique cannot be used.

An alternative is the use of a large bolus dose of vecuronium which prolongs its duration of action. We administered an $ED_{95} \times 8$ dose (28 mg) of vecuronium and have demonstrated that even this very large bolus did not cause any cardiovascular effects and provided satisfactory relaxation for the entire procedure.

The use of isoflurane for anaesthesia in patients with phaeochromocytoma has been well documented.[26–28] Previous authors have commented on the stability of cardiac rhythm during isoflurane anaesthesia for removal of catecholamine-secreting tumours. Neither of our patients had any disturbances of cardiac rhythm, other than sinus tachycardia, at any time. This included, in both patients, the period of tumour manipulation, when the sudden increase in arterial pressure (despite adequate pre-operative α- and β-blockade) suggests that circulating catecholamine levels must have been substantially increased. A further advantage of isoflurane is that it is a potent vasodilator, and because of its low blood/gas partition coefficient, rapidly reversible changes in systemic vascular resistance and thus in arterial blood pressure can be attained. In a sense it may be termed 'inhalational sodium nitroprusside'.

The patient in Case 1 had required treatment with α-methyl-para-tyrosine[8,29] to control his hypertension. This is a competitive inhibitor of tyrosine hydroxylase which acts centrally as well as in the periphery. This enzyme is the rate-limiting step in catecholamine synthesis. In patients with phaeochromocytoma, treatment reduces daily catecholamine synthesis by 20–80%. Either on its own, or in combination with phenoxybenzamine it usually produces adequate control of blood pressure and of symptoms and has been used for the treatment of patients with malignant phaeochromocytoma not amenable to surgical excision.[8,29]

Alpha-methyl-para-tyrosine has two side effects of anaesthetic importance. First, it can potentiate the extrapyramidal side effects of butyrophenones (e.g. droperidol) and second it may cause sedation, which will potentiate the effects of other central nervous system depressants. Occasionally, psychic stimulation may occur and our patient was restless and agitated pre-operatively. It was interesting that he was very heavily sedated following premedication, even though similar premedication with his previous anaesthetic had been described as inadequate. Phenoxybenzamine is also reported to cause sedation,[30] so that the precise nature of the interaction is difficult to interpret. Whatever the cause, it seems likely that his prolonged period of peri-operative sedation and hence relative immobility was a contributory factor to his postoperative pulmonary complications.

In summary, we have described two techniques for administering vecuronium to patients anaesthetised for removal of phaeochromocytoma. Both were very satisfactory in the cases described and the choice of technique may be influenced by the availability of infusion devices and of methods of monitoring neuromuscular transmission. If such devices are not available, we suggest that the use of a large bolus dose (0.4 mg/kg, $ED_{95} \times 8$) will produce prolonged surgical relaxation. In our patient, even this very large dose of vecuronium was without cardiovascular side effects. We suggest that whatever the method of administration, vecuronium is probably the muscle relaxant of choice in patients presenting for the removal of a phaeochromocytoma.

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APPARATUS

Patient-controlled analgesia

Experience of two new machines

H. OWEN, R. J. GLAVIN, R. M. REEKIE AND A. S. TREW

Summary

Two modern patient-controlled analgesia pumps have been evaluated in the laboratory and in clinical use. Both machines generally performed satisfactorily and patients achieved good pain relief from self-administered morphine. The relative merits of the two pumps are discussed and although the on demand analgesic computer is preferred, a substantial investment of time on the ward is required to provide continuous patient-controlled analgesia.

Key words

Pain; postoperative.
Equipment; infusion pumps.

The technique of patient-controlled analgesia (PCA) has been used for over 20 years,[1] but was first employed after surgery to provide an objective measurement of pain.[2] In this early system, demands for analgesia were made by pressing a button and the analgesic was administered intravenously by a nurse–observer, who also recorded its effect. Manual administration of drug has been replaced by increasingly sophisticated syringe pumps.[3-7] The latest are compact microprocessor-controlled devices with controls for the prescription of incremental and total doses, lockout time, speed of injection and background infusion rate.[8]

The only system in production available at the time of this study in the UK was the On Demand Analgesia Computer (ODAC, Janssen Scientific Instruments, Beerse, Belgium) but the Harvard PCA system (C.R. Bard Inc., New Jersey) is available in the USA. This paper presents a clinical and laboratory assessment of the ODAC and Harvard PCA machines*.

Description of PCA pumps

On demand analgesia computer (Fig. 1)

ODAC is a self-filling syringe drive mechanism and microprocessor control unit, mounted on a stable base with overall dimensions of 40.5 × 30.7 × 31 cm and weighing 13 kg. On the control unit is a bank of three illuminated buttons indicating and controlling power (on/off, mains/battery), unit operation (run/stop) and alarm (on/off). The demand dose (0.1–5 ml), background infusion rate (0.01–0.99 ml/minute) and

*The ODAC is distributed by Sonicard Ltd, Quarry Lane, Chichester; Harvard PCA is distributed by Bard Ltd, Pennywell Industrial Estate, Sunderland.

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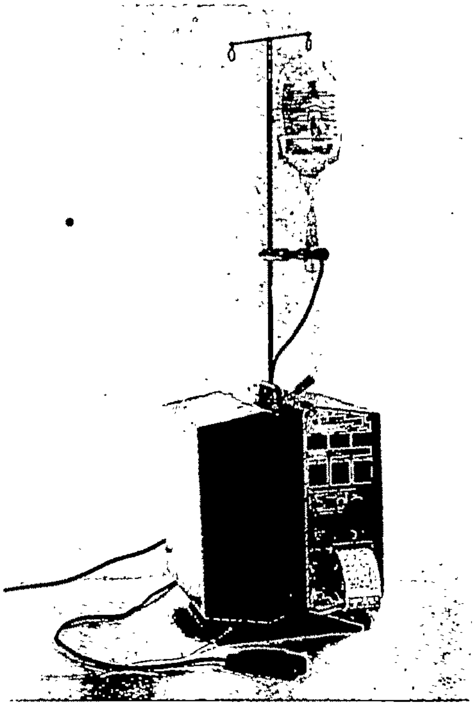

Fig. 1.

maximum dose (1–99 ml/hour) are set by thumbwheel switches. The background infusion can be fixed or adaptive (automatically varied in response to demands). The lockout interval and concentration of drug used are set by turning screws located behind a perspex cover. A semi-permanent copy of operation by ODAC is produced by an integral printer on thermosensitive paper and a continuous record of all demands made, demands granted and alarm or fault conditions can be obtained. A cumulative report and a graph of demands against time can also be printed.

The infusion controller requires a unique disposable giving set for correct operation. This includes a drip chamber of dimensions to fit the supply detector, a one-way valve assembly to allow the syringe to be refilled automatically, a syringe of special dimensions and a length of flexible tubing to fit the air detector.

The syringe is driven by a stepping motor and the position of the plunger is checked both mechanically and electro-optically using a series of LED's. The syringe is protected behind a transparent door and unauthorised access triggers an alarm. Other alarms include empty drug supply, air in tubing, low battery, maximum dose and excessive syringe friction (or blocked tubing). If the alarm operates, the ODAC automatically shuts down.

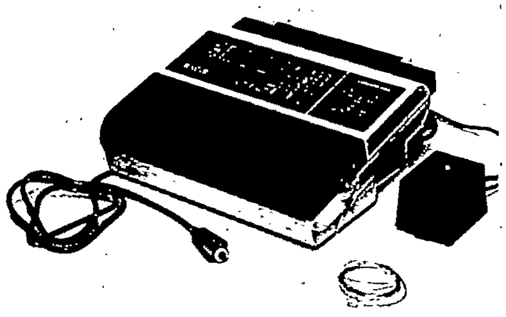

Fig. 2.

Demands are made by pressing a recessed button on the handset; a successful demand for analgesia requires two button presses within one second. Audible confirmations of all demands are made and successful demands are specifically acknowledged. Pilot lights in the control unit indicate when demands will, or will not, be granted.

Harvard PCA (Fig. 2)

This device is a single unit of dimensions 32 × 25.5 × 11.5 cm and weighing 4.55 kg. A key is required to turn the device on and off and three small pilot lights indicate power on, battery back-up in use and alarm. The demand dose (0.1–10 ml) and lockout interval (3–70 minutes) are entered using a sealed membrane key pad. The device can administer a constant rate infusion or on-demand analgesia. Demands are made by pressing the prominent button on the handset. Only a single button press is required and a chime acknowledges all demands.

Information on settings and demands, both successful and unsuccessful, can be obtained from an alphanumeric LCD message panel by entering a security code. This operation also allows the settings to be changed. A printer is under development by Bard. Specific types of 60-ml syringes are required for accurate performance and a 'tamper-resistant microbore extension set' is recommended by the manufacturers. In use, the syringe is protected behind a lockable tinted perspex cover.

Table 1. Accuracy of ODAC and Harvard PCA. Values are mean (SD as a percentage of mean) and range

	Bolus dose delivered (ml)	Infusion rate delivered	
ODAC Prescribed dose 5 ml		0.01 ml/minute	0.15 ml/minute
A	4.72 (0.6)	0.0107 (4.1)	0.140 (3.7)
	4.67–4.76	0.0096–0.0111	0.1312–0.1477
B	4.86 (0.4)	0.0088 (22.5)	0.141 (5.8)
	4.83–4.89	0.0067–0.0117	0.1271–0.1490
C	4.92 (1.2)	0.0106 (4.9)	0.148 (1.8)
	4.78–4.99	0.0101–0.0113	0.1432–0.1520
Harvard Prescribed dose 1 ml PCA		2 ml/hour	
	0.88 (6.0)	1.96 (2.9)	
	0.82–0.99	1.88–2.08	

Alarm functions include unauthorised attempts to alter settings or gain access to the syringe compartment, blocked line, nearly empty (5 ml left) and empty syringe, electronics fault, low battery and maximum dose.

Methods

The laboratory and clinical evaluations were carried out over 6 months on two ODAC's purchased by the department, one ODAC loaned by the suppliers in the UK and on one Harvard PCA loaned by the manufacturers.

Laboratory assessment

Electrical safety. Equipment was tested to BS5724 requirements[9] using a Rigel 232 electrical safety tester.

Accuracy of bolus dose plus infusion rate. The accuracy of the bolus dose was measured gravimetrically 20 times on each machine. The volume settings were those used clinically (ODAC: 5 ml, Harvard PCA: 1 ml). The accuracy of infusion rates was measured gravimetrically 10 times on each machine. The infusion rates chosen were those we have used clinically (ODAC: 0.01 ml/minute and 0.15 ml/minute, Harvard PCA: 2 ml/hour). The infusate was glucose 5%.

Noise. The noise produced at 0.5 m during normal operation by the ODAC printer and by the alarms was measured using a precision sound meter (Bruel and Kjaer Model No. 2203).

Self-contained power supply. After being charged for over 24 hours, each machine was operated on its batteries with simulated demands being made until a low battery message appeared.

Clinical assessment

After a 3-week trial period the four units were used on several surgical wards for 6 months. All patients received increments of morphine (1 mg) in glucose 5% by PCA for 24 hours postoperatively. Full records of performance of the machine and the behaviour of patients were made for the Harvard PCA ($n=26$) and ODAC ($n=124$). Comments on the machines were prompted from both patients and nurses and a verbal pain rating (no pain, mild pain, moderate pain, severe pain) was recorded from all patients.

Results

Laboratory assessment

Electrical safety. The ODAC units are manufactured to category BF, but on initial testing only one unit complied with BS5724. The protective metal covers of the other two ODAC's were poorly earthed. This was due to paint insulating earth straps; once discovered this was easily rectified. The covers do not provide protection against ingress of fluid from a leaking infusion bag.

The category mark required by BS5724 was not present with the Harvard PCA equipment. When tested through the charging unit, the other requirements of this standard were met.

Accuracy of bolus dose and infusion rate. All units failed to deliver the volumes prescribed (Table 1), but were within the manufacturers' stated tolerances. The standard deviation is presented as a percentage of the mean to give an indication of the accuracy which can be expected, e.g. on 67% of occasions ODAC A will deliver within 0.6% of 4.72 ml when 5 ml has been prescribed.

Noise. The background noise level in a ward is 40–50 dB. The noise produced by normal operation and by infusion was below this level in all machines, although the ODAC printers produced a transient level of 62–69 dB. The Harvard PCA delivered the incremental dose very quietly, but the ODAC's produced 54–60 dB. The note acknowledging a demand was 66 dB from the Harvard PCA and that from the ODAC was adjustable from 0–80 dB. The Harvard alarm consists of three chimes of 80 dB. The ODAC alarm was much quieter at 52 dB, but continues until the alarm is cancelled.

Self-contained power supply. The ODAC functioned on batteries for 30–35 minutes regardless of the number of demands made. The Harvard PCA continued to operate for 4.5–5.5 hours depending on the number of demands made.

Clinical assessment

ODAC. The faults recorded by the ODAC in 124 patients using PCA for 24 hours after surgery, are listed in Table 2. The 'door unlocked' alarm always followed another fault and so was associated with correction of a previous fault and not with unauthorised access to the syringe compartment. This fault, and maximum dose (which is not due to failure of equipment) have not been considered further. A fault which required action to be taken by medical or nursing staff occurred every 5.6 hours, a rate of approximately one fault for every 10 successful demands for analgesia. In only 33 cases was the 24 hours uncomplicated and in 77 cases there were between one and 10 faults in the 24 hours. In four cases more than one fault occurred every hour, and in three cases the ODAC failed completely and had to be replaced. The ODAC's were set to administer 1 mg increments of morphine on demand with a lockout time of two minutes. Of 124 patients, only 22 experienced more than mild pain and most were satisfied with PCA. The handset rested comfortably in the hand and because of the Velcro fastening rarely got lost in the bed. All patients were able to make the two button presses required for a successful demand.

Table 2. Alarm conditions recorded by ODAC during administration of PCA to 124 patients

Fault	Number of occurrences
Air in tubing	264
Supply error	256
Maximum dose	121
Door unlocked	74
Valve friction	6
Syringe friction	2
Low battery	1
Unknown	3

If the intravenous cannula became blocked or the delivery tubing was kinked, the tubing occasionally became disconnected at a rubber–plastic joint before enough pressure had developed to cause an alarm. This obviously opens the demand feedback loop and resulted in at least one high pain score. The special giving set caused much frustration. Extreme care is required during priming to avoid the inclusion of air bubbles and approximately 10% of the first 100 giving sets had been poorly assembled and leaked. A change in the manufacture of the giving sets has been made and we have had no problems with them since then.

In an unplanned drop-test, one ODAC survived a fall of 0.9 metres intact, apart from a damaged base plate.

Harvard PCA. Only a total of six faults occurred during use of the device on patients in the first 24 hours after surgery. On three occasions the device shut down for no apparent reason and required repeat of the start-up procedure. On one occasion it was not possible to open the cover to change an empty syringe and PCA had to be discontinued. This was because the mains supply to the unit had been inadvertently switched off and the battery was unable to supply enough power to the unlocking solenoids. The other faults were failure of internal switching between mains and battery back-up power supply and the 'Watchdog error' message which appeared 12 hours later because a fault had been detected in the pump's electronic circuitry. These latter faults required the device to be returned to the supplier for inspection and repair.

The Harvard PCA was generally satisfactory in use. Increments of morphine 1 mg were prescribed with the minimum lockout time of 3 minutes, and no patient had more than mild pain postoperatively, although the small handset on a short lead was sometimes mislaid in the bed. The pump was easily loaded and reloaded by nursing staff. A key is required for this and the key also allows access to the security code and the opportunity to change the PCA settings. The security code is also required to access data on settings and demands. When the security code is entered the first message to appear includes the opportunity to change settings with a single key press. Settings were inadvertently changed twice. The internal memory can only store a limited amount of data and when PCA was used for more than 24 hours, data on demands made from the first hours of use were deleted to include the most recent data.

Discussion

The ODAC and Harvard PCA pumps performed satisfactorily in both laboratory and clinical practice. Using these devices, good pain relief was achieved after abdominal surgery with small increments of self-administered morphine. Although generally adequate in design, both manufacturers could substantially improve their products. Poor quality control resulted in only one of the three ODAC's satisfying the requirements of BS5724, but the manufacturers have assured us that in all future ODAC's this fault will be rectified. The Harvard PCA will require the 'BF' category mark before going on sale.

All the devices failed to deliver the prescribed volumes, although not by more than the manufacturer's tolerances. This should not affect the provision of pain relief because another demand can be made whenever required. The alarms are comprehensive on both machines and both are 'user friendly'. The ODAC prints out the fault and the Harvard PCA displays the appropriate message. The alarm of the Harvard PCA can easily be missed because after sounding three chimes there is only a small red warning light indicating a fault. The larger flashing illuminated button of the ODAC is preferred.

The Harvard PCA chimes in acknowledgment of both successful and unsuccessful demands and operation of the pump can only be checked by entering the security code and asking for the number of demands to be displayed. The ODAC acknowledges all demands and specifically acknowledges successful demands. This auditory feedback was appreciated by many of the patients and the volume can be increased enough to be heard by attending staff throughout the ward.

The handset of the ODAC was easily managed by all patients, even though two button presses are required in quick succession. It is large enough to be gripped and the recessed button needs little displacement to operate it. The Harvard PCA has a button similar to that of some slide projectors and was generally disliked. The button is proud of the handset and one demand was granted after it was dropped out of bed by the patient.

The self-contained power supplies of the pumps facilitate the transfer of patients from a recovery ward to the general ward and for continued pain relief if power supplies are interrupted. It is much easier to transport the smaller Harvard PCA between wards.

PCA has been claimed to reduce time spent by nursing staff in administering analgesia.[10,11] We have not been able to confirm this. Patients need instruction in the use of the machines preoperatively for best results. The PCA pumps need to be loaded with analgesic and this still requires two nurses to check the prescription of a controlled drug before starting therapy. Once running, we have found that intervention to continue PCA by ODAC is required at least every 6 hours and this often takes as long as administering an intramuscular injection. It has already been shown that regular administration of an analgesic is at least as good as PCA[12] and on time saving alone we cannot recommend PCA.

There is a poor correlation between nurses' observations and patients' self reports of pain.[13] The common factor in PCA and regular administration of analgesia is that nursing staff do not need to decide when analgesia is required.

The ODAC is much more flexible than the Harvard PCA pump. The ODAC can administer a background infusion of analgesic which can be set to reflect the number of demands made by the patient, although there is no evidence that this improves pain relief. The three-minute lockout interval of the Harvard is unnecessarily restricting, as is the fixed limit of five demands granted in an hour, although this can be over-ridden.

Morphine consumption by patients can be readily recalled from ODAC. Without knowledge of the security code this information is unavailable from the Harvard PCA and the volume left in the syringe is almost invisible behind the smoked perspex cover. Addition of the printer to the Harvard PCA increases its size and cost substantially.

Both the PCA models studied cost in excess of £3000 (including VAT) which probably reflects research and development costs. Other medical equipment manufacturers are developing PCA pumps and it is anticipated that some of these will be significantly cheaper, e.g. the Graseby PCAS*. When considering the cost of introducing PCA, savings in specialised nursing time have been claimed to offset the expenditure.[11] Even after an initial familiarisation of nursing staff with PCA, we have not been able to confirm this saving in nursing or medical time.

*Graseby PCAS distributed by Graseby Medical Ltd, Units 3–4, Odhams Trading Estate, St Albans Road, Watford, Herts.

Acknowledgments

The authors wish to thank Bard Limited and Sonicaid Limited, each for the loan of their PCA system, and Mr J. McGarrity and Mr K. Carter of the Department of Medical Physics at the Royal Infirmary for their technical help. Sister S. Blackwood and the nursing staff of Ward 33 at the Infirmary have all been extremely helpful and have made many useful comments which have been utilised in the preparation of this paper.

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Anaesthesia, 1986, Volume 41, pages 1236–1239

APPARATUS

A disposable device for infusion analgesia

An evaluation of the Travenol infusor

R. M. REEKIE, K. B. CARTER AND H. OWEN

Summary

The performance of the Travenol infusor when used to administer an intravenous infusion of analgesic after surgery has been investigated. Mean flow was very similar to the manufacturer's quoted figure of 2 ml/hour, but there was a large interindividual variation. Results from a laboratory study suggest that this was due to variation in the manufacture of the infusor.

Key words

Equipment; infusors.

A compact disposable device able to deliver a constant fixed rate intravenous infusion has recently been marketed in the United Kingdom (Travenol Laboratories Ltd, Norfolk). The Travenol infusor was designed for administration of chemotherapeutic agents to ambulant patients,[1,2] but has also been used to provide postoperative pain relief.[3] Factors such as temperature, position of the device and even gender of the patient have been found to affect the infusion rate.[4] This is a report on the performance of infusors used peri-operatively, together with a laboratory evaluation.

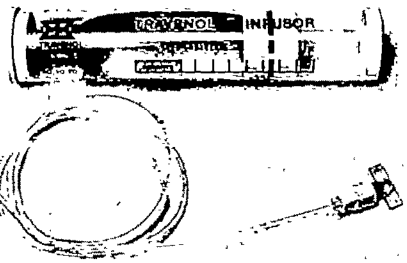

Fig. 1. The Travenol infusor (this device is partly discharged and the winged luer cap at the end of the delivery tubing is to stop flow).

Methods

Description of infusor

The Travenol infusor (Fig. 1) consists of an elastomeric balloon of capacity 60 ml, enclosed in a semirigid transparent casing. The balloon is filled through an injection port which has a marker to indicate fluid volume. Flow through

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kink-resistant delivery tubing starts as soon as it is filled; power is provided by the energy stored in the balloon. The infusor has been designed so that when filled with glucose 5% and maintained close to body temperature an orifice restricts flow to 2 ml/hour (±10%).

Technique of testing

The flow of three infusors filled with 60 ml glucose 5% was determined for 30 hours. Each infusor was placed in an oven held at 35°C (SD 0.2); pressure in the reservoir balloon was measured through the filling port using a Gould pressure transducer and recorded on a chart recorder. The infusate was collected by an LKB Ultrarac fraction collector set to change sampling tubes every hour. The volume delivered each hour was calculated from the increase in weight of the sampling tube. Evaporation losses were determined from filled dummy tubes in the fraction collector.

The effect of changes in pressure on flow was investigated by re-introducing small volumes of glucose 5% into the balloon to recreate a range of pressures. Flow was determined by measuring the time taken for the infusor to deliver 0.05 ml into a 0.1 ml pipette. Flow was also measured in two infusors subjected to temperatures between 22°C and 35°C in a water bath.

Sixty-two consecutive patients with no serious intercurrent disease, scheduled to undergo abdominal surgery, received postoperative analgesia by constant rate infusion from an infusor filled with a solution of either ketamine or morphine in glucose 5%, and connected to an intravenous cannula (20 gauge). Soon after anaesthesia was induced, all patients received a bolus of the analgesic agent followed by the infusion. The infusor was placed in contact with the patient's body, under drapes, during surgery and was covered by bedclothes postoperatively. After approximately 24 hours, the analgesic infusion was stopped and the volume remaining in the infusor aspirated and measured. Mean flow was calculated from the following equation:

$$\frac{60 - \text{residual volume}}{\text{infusion time (hours)}} = \text{mean flow (ml/hour)}$$

The difference in flow between male and female patients was compared using an unpaired Student's t-test.

Table 1. Flows from three infusors at 35°C

Infusor no.	Mean flow over 24 hours (ml/hour)	Minimum flow over 1 hour (ml/hour)	Maximum calculated flow (ml/hour)
1	2.09	1.58	3.7
2	2.07	1.82	3.5
3	3.10	1.90	3.5

Results

Infusion rates and pressures in the three devices followed a similar pattern to that shown in Fig. 2. The flow is low for the first hour and is then fairly constant for 24 hours. Pressure falls quickly in the first few hours and then declines more gradually, until less than 10 ml remain in the reservoir. Thereafter, both pressure and flow increase rapidly until only 2 ml remain. Minimum and mean flows over 24 hours for the three infusors are given in Table 1.

When the pressure inside the balloon was manipulated, it was found that flow was proportional to applied pressure over the working range. After 24 hours the pressure inside the balloon rises and flow increases (Fig. 2). The measured flow was averaged over each hour and the maximum flow which would have occurred was calculated from the peak pressure recorded (Table 1).

The effect of change in temperature on flow is given in Table 2. Pressure within the balloon changed very little with changes in temperature

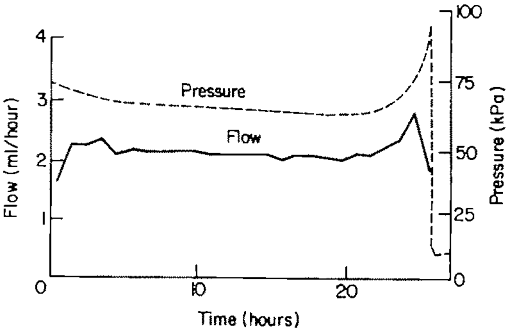

Fig. 2. Flows and pressures recorded over 30 hours from a typical infusor at 35°C. ---, Pressure; ——, flow.

Table 2. Effect of changes in temperature on flow from two infusors

Infusor no. 4		Infusor no. 5	
Temperature (°C)	Flow (ml/hour)	Temperture (°C)	Flow (ml/hour)
22.0	1.55	22.5	1.57
28.5	1.76	27.8	1.75
35.0	1.98	35.0	2.11

Table 3. The range of mean flows obtained from 61 infusors

Flow (ml/hour)	*n*
1.4–1.59	3
1.6–1.79	3
1.8–1.99	31
2.0–2.19	19
2.2–2.39	4
2.4–2.59	1

(100 Pa/°C); however, flow increased linearly with temperature by 0.033 ml/hour/°C.

Of the 63 infusors which were used clinically, one burst during filling and a second failed to prime itself. Data from the 61 devices used after surgery are presented in Table 3. We have found a mean flow of 1.97 ml/hour (SD 0.18, range 1.41–2.42 ml/hour). Mean flows were the same in males and females.

Discussion

Seventy-two per cent of infusors used clinically achieved flows within 10% of 2 ml/hour. During surgery, skin temperature falls by approximately 0.3°C/hour and a large fall is seen during transfer to the recovery room.[5] However, this would account for a decrease in the flow of less than 0.1 ml/hour and it would require a sustained fall in temperature of 15°C to reduce flow to the lowest values recorded. This was unlikely because all infusors were kept in close thermal contact with patients. A large increase in temperature of similar magnitude would be required to produce the highest infusion rates measured. We conclude, therefore, that most infusion rates outside 2 ml/hour (± 10%) are caused by variations in manufacture.

The laboratory data shows the importance of correct and constant temperature for the satisfactory performance of the infusor. When moved from room temperature to body temperature the device warms up slowly and flow increases. This is due mainly to reduced viscosity of the balloon contents. Under constant temperature conditions, flow is then fairly constant, but after 24 hours, when approximately 6 ml remain, flow increases rapidly due to an increase in pressure (Fig. 1). A peak flow in excess of 1.5 times the design flow can be expected and this agrees with the manufacturer's recommendation that each infusor should only be used for 24 hours. One infusor failed to prime itself. This is a fault which is acknowledged by the manufacturer and can be caused by an air lock in the flow restrictor or failure of the solution to wet an internal filter.

The fixed rate limits the usefulness of the device in providing infusion analgesia after surgery and since each costs approximately £25 (for a single use) it is unlikely to be widely adopted for this purpose in hospitals when syringe pumps are available. It is, however, robust, light and self powered and is well suited for intravenous therapy in ambulant patients. It could be very useful in providing constant rate infusions for analgesia or sedation during transportation of patients between hospitals.

Acknowledgments

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Anaesthesia, 1986, Volume 41, pages 1240–1250

SPECIAL ARTICLE

Obstetric epidural test doses

A reappraisal

G. PRINCE AND D. MCGREGOR

Summary

A number of obstetric fatalities related to epidural anaesthesia have been reported recently. In each case catheter or needle misplacement had resulted in a lethal intrathecal or intravascular injection. In this review these cases and a number of other similar but nonfatal reports are examined. In many cases, essential safety checks such as the aspiration test and the test dose had not been performed before the epidural injection, but in others one or both of these tests had been used and had failed to predict the complication. Safety test failures generally occurred because ineffective tests were used or because effective tests were inadequately interpreted. This is not surprising because although textbooks recommend a bewildering variety of test doses, they seldom give precise details as to how they should be conducted. A detailed test dose protocol is recommended, which will safely warn of epidural catheter and needle misplacement in the most effective manner possible. If the protocol is used, accidental subarachnoid and intravascular injections can be reduced to a minimum, but they will still occur. It is emphasised that these complications should not cause fatalities if trained personnel and adequate resuscitation facilities are available.

Key words

Anaesthetic techniques, regional; epidural.

In the early years of this century, the subarachnoid injection of large quantities of local anaesthetic to produce total spinal anaesthesia enjoyed a short vogue[1] which rapidly disappeared following the discovery that respiration was frequently jeopardised, sometimes with fatal results.[2,3] Dogliotti was obviously aware of this when he first described the injection of large volumes of local anaesthetic to produce lumbar epidural anaesthesia in 1933.[4] He suggested an aspiration test followed by the injection of a test dose to exclude subarachnoid placement of the needle. Many anaesthetists have such confidence in the effectiveness of these safety tests that they commence obstetric epidural anaesthetics, while unprepared to deal with their possible consequences. This problem has led at least one author to recommend abandonment of test doses altogether.[5]

Is the test dose necessary?

In units where epidurals are available on demand, as many as 40% of parturients request one and a 60% epidural Caesarean section rate can be obtained.[6] The test dose is designed to avoid two potentially lethal complications of epidural blockade, namely total spinal block and accidental intravascular injection of local anaesthetic. In large reviews, the incidence of each of these complications is between 3 and 10 per 10 000 epidurals.[7-10]

Total spinal block

If a large volume of local anaesthetic intended for the epidural space is injected into the subarachnoid space, severe hypotension, coma and complete paralysis with fixed dilated pupils

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develop over a period of 5–10 minutes following injection and may last several hours. In general surgical practice this is seldom a life-threatening problem. The first 17 cases reported in the literature recovered fully after prompt tracheal intubation, ventilation and fluid resuscitation.[11] The obstetric patient is at greater risk; hypoxia ensues rapidly when ventilation becomes inadequate and soiling of the lungs by highly acid stomach contents is likely to occur. There have been three fatalities in the United Kingdom since 1984 following total spinal blocks in pregnant women. These cases were the subject of considerable attention in the national press.[12]

Accidental intravascular injection

Massive intravascular injection of local anaesthetic in a labouring woman will result in jitteriness, tinnitus and, eventually, convulsions. This will accelerate the onset of hypoxia and acidosis.[13] As with total spinal block, vomiting and aspiration may occur. Until recently it was thought that rapid intubation using suxamethonium and assisted ventilation with 100% oxygen could avert disaster but in 1979, Albright[14] suggested that highly lipid soluble and protein bound local anaesthetics such as bupivacaine and etidocaine may be uniquely cardiotoxic when injected as a bolus intravenously. This claim was initially substantiated with six case reports, but data on 33 cases of cardiac collapse following inadvertent intravenous injection have since been published. Amongst these there are 22 cases of maternal cardiac arrest after bupivacaine, 15 of them fatal.[15] Some of these followed as little as 60 mg of bupivacaine. Animal research has confirmed these findings.[16–19] As a result, 0.75% bupivacaine is no longer used in obstetrics, but 0.5% bupivacaine in the type of dose commonly used for epidural Caesarean section has caused ventricular tachydysrhythmias, cardiac decompensation and death when injected rapidly into an epidural vein.[15]

Safety standards for nonepidural obstetric anaesthesia and analgesia are extremely high. No deaths directly resulting from inhalational or pethidine analgesia in labour have occurred in the twenty million maternities studied by the Confidential Enquiry into Maternal Mortality and less than 1 in 5000 mothers given a general anaesthetic for Caesarean section will perish as a result of aspiration or hypoxia.[20] If we cannot at least match these standards in our epidural services, demand for the technique will surely diminish. To this end it is recommended that, prior to the injection of local anaesthetic into the epidural space, a two-stage safety check is performed. It should consist of aspiration to detect blood or cerebrospinal fluid (CSF) and a test dose injection of local anaesthetic, which may or may not contain a small quantity of adrenaline and observation of the effects of the injection for 5 minutes. There is ample evidence that these tests can reduce the incidence of accidental total spinal blocks and intravenous injections[8,21–23] and that the use of both tests is more effective than either is alone.[21,22,24]

Unfortunately, despite these methods being recommended in nearly every textbook of obstetric anaesthesia, intravascular and intrathecal injections continue to occur. Sometimes this is because the anaesthetist has decided that a test dose is unnecessary or unsafe; on other occasions the test dose has been given but in such a way as to render it ineffective. We have already indicated that safety checks are necessary prior to epidural local anaesthetic injection and the remainder of this review will show how the safety and effectiveness of these checks can be used to maximum advantage.

Is the obstetric epidural test dose safe?

No major complications, apart from test dose failure and its consequences, have been ascribed to an obstetric epidural test dose, but a number of possible problems have profoundly influenced anaesthetists in their choice of agent. Adrenaline in particular is still widely avoided because of its alleged potential for causing neurological damage. In fact there is a large body of evidence supporting its safety. This problem and others which affect the welfare of mother or fetus are reviewed below.

High spinal blocks

A number of reports have appeared where the injection of 3–4 ml of isobaric 0.5% bupivacaine into the subarachnoid space to produce spinal anaesthesia for Caesarean section has resulted in a high or total spinal block.[25–27] This occurs because transient aortocaval compression during positioning increases extradural space pressure,[28] causing the CSF and local anaesthetic to move rostrally.[29,30]

The patient having an epidural block is usually positioned prior to the test dose injection, so high blocks should be uncommon, but sensible precautions must be taken. If isobaric solutions are used, patients should not be moved until it is certain that the test dose has not been injected intrathecally; if a subarachnoid injection does occur the patient must remain still for at least 40 minutes.[30] Unnecessarily large volumes of local anaesthetic should be avoided. If 1.5–2 ml of isobaric 0.5% bupivacaine is used anaesthesia is adequate for Caesarean section and high blocks do not occur.[31] If a hyperbaric test dose solution is used patient movement is safe at any time, provided slight head-up tilt is maintained and a sensible volume of test dose is chosen. Effective solutions can all produce an adequate block using volumes of 2 ml or less.[32,33]

Adrenaline and anterior spinal artery thrombosis

In the late 1950s and early 1960s a number of papers were published which claimed that the inclusion of adrenaline in solutions injected into the subarachnoid space had resulted in paraplegia secondary to anterior spinal artery thrombosis.[34,35] In the UK, many anaesthetists had abandoned subarachnoid anaesthesia altogether following the Woolley and Roe court case[36] and those that had not were quick to stop using adrenaline in both epidural and spinal blocks.

There is, however, little evidence that epidural or intrathecal adrenaline is dangerous in obstetric patients; paraplegias are easily explained by alternative pathologies such as adhesive arachnoiditis or trauma. The twelve patients reported by Davies *et al.*[34] and Catterberg and Insausti[35] were in an older age group (mean age 64 years). This is of great importance; with increasing age the anterior spinal artery becomes increasingly tortuous and fibrosed.[37] If hypotension occurs, these patients are at risk from paraplegia whether adrenaline has been used or not. Some authors have injected massive doses of adrenaline intrathecally in pregnant women without long term sequelae[38,39] and animal studies suggest that spinal blood flow is unaffected by intrathecal[40,41] and increased by intravascular adrenaline.[42] We conclude that there is no evidence that small quantities of adrenaline can cause anterior spinal artery spasm or thrombosis in the obstetric population. Its inclusion in the test dose is vital if large quantities of local anaesthetic are to be used.

The test dose and placental blood flow

Fetal wellbeing depends on an adequate supply of oxygenated blood to the placenta. In normal pregnancies placental blood flow (PBF) is 500–750 ml/minute at term, but in patients with pre-eclampsia, diabetes and intra-uterine growth retardation it is often dramatically reduced. Fortunately, the fetus can survive with half the normal mean blood flow,[43] but problems do arise during labour in these patients because uterine contractions cause further transient falls in placental flow and fetal distress may result. Drugs causing placental vasoconstriction will exacerbate these problems and they should be avoided in patients with placental insufficiency. Though local anaesthetics do constrict the uterine vessels, the effect is insignificant unless toxic doses are administered.[44,45] Adrenaline is a powerful placental vasoconstrictor,[46,47] but it has little effect on placental blood flow when injected epidurally or intrathecally.[48,49] An intravenous injection, however, does affect placental flow. A 15 μg test dose was injected as a bolus intravenously into pregnant ewes and a 50% fall in uterine blood flow lasting 3 minutes was observed.[50] Similar falls in a patient with placental insufficiency could be dangerous and we recommend that adrenaline should not be used in the test dose if there is any question as to the adequacy of placental blood supply.

Can intravenous injection of the test dose cause maternal cardiac dysrhythmias?

A 2-ml test dose could contain a maximum of 10 mg of bupivacaine (0.5%) or 100 mg of lignocaine (5% heavy). This dose of either drug would not be expected to have any cardiac effects. Lignocaine depresses myocardial function in a dose dependent manner, but does not cause significant effects until well above the seizure threshold. Bupivacaine may cause cardiac dysrhythmias at concentrations below the seizure threshold,[16,17] but in humans complications have not been seen unless more than 60 mg have been injected intravenously.[15]

Table 1. Published cases of total spinal block and intravascular injections. Aspiration test failure

Author	Number of cases	Reason for block	Therapeutic injection	Aspiration test	Outcome	Likely cause of aspiration test failure
Bonica *et al.*[23]	1	General surgery	Through needle	Through needle	Total spinal block	Needle blockage
Gavin[24]	1	General surgery	Through catheter	Through needle	Total spinal block	Dural puncture during catheter insertion
Gillies and Morgan[58]	2	General surgery	Through needle	Through needle	Total spinal block after failed test dose	Needle blockage
Kenepp and Gutsche[22]	33	Obstetric pain relief	Through catheter	Through catheter	Mild toxicity	Catheter blockage
	5		Through catheter	Through catheter	Convulsions	Catheter blockage
Moore *et al.*[13]	2	General surgery	Through needle	Through needle	Convulsions after failed test dose	Needle blockage
Soni *et al.*[21]	2	General surgery	Through catheter	Through catheter	Test dose prevented i.v. injection	Catheter blockage

Table 2. Published cases of total spinal block and intravascular injection. Test dose failure

Author	Number of cases	Reason for block	Details of test dose	Complication	Result	Likely reason for test dose failure
Gillies and Morgan[58]	2	General surgery	2 ml bupivacaine 0.5% with 1:200 000 adrenaline	Intrathecal injection	Total spinal block	Slow onset of spinal block with bupivacaine
Kenepp and Gutsche[22]	51	Obstetric pain relief	2 ml local anaesthetic	Intravenous injection	Convulsion 5 cases, tremor 34 cases No effect in 11 cases (blood aspirated after therapeutic dose)	Local anaesthetic test dose produced symptoms of intravenous injection in only 3% of cases
Moore *et al.*[13]	2	General surgery	3 ml local anaesthetic with 1:200 000 adrenaline	Intravenous injection	Convulsion	Patient heavily sedated No ECG monitoring
Soni *et al.*[21]	1	General surgery	3 ml local anaesthetic with 1:200 000 adrenaline	Intravenous injection	Convulsion	Patient β-blocked and sedated so adrenaline produced no effect
Albright[15]	6	Obstetric pain relief	Local anaesthetic test doses of 2–5 ml 0.75% bupivacaine	Intravenous injection	Cardiotoxicity and death	Even large doses of local anaesthetic do not cause symptoms on intravenous injection

Early workers with adrenaline quickly showed that large bolus injections caused cardiac dysrhythmias and death in animals,[51] but wide species variation makes it difficult to define a therapeutic ratio for man. In a study of 175 heavily premedicated surgical patients given a bolus of 15 μg of adrenaline, dysrhythmias, which occurred in 50% of those studied, were universally benign.[52] In the younger obstetric population an even lower incidence would be expected.

Is the obstetric epidural test dose effective?

It is generally accepted that a test dose should be interpreted within 5 minutes of injection, but there is far less agreement over what it should consist of.[7,11,23,31,52-57] Examination of published case histories reporting accidental total spinal blocks and intravascular injections (Tables 1 and 2) reveals that some are less effective than others; this experience can be used to suggest ways of improving the success rate of the aspiration test and the test dose.

The aspiration test

If aspiration was always effective there would be no need for a test dose. In fact there are four major causes of aspiration test failure (Table 1); all of them are to some extent avoidable.

Blockage. The epidural catheter can easily be blocked by blood or tissue, making aspiration impossible.[21,22] It is less common for the needle to be blocked, but there are case reports of intravascular[13] and intrathecal[58] injections through the needle following negative aspiration tests.

Vessel or dural puncture during catheter insertion. Vessel puncture on catheter insertion has been reported in as many as 9% of obstetric epidurals.[59] Dural puncture in this way is far less common, but has been reported.[24,60] Neither aspiration nor the test dose can be effective if they are done through the needle before the catheter is passed.[61]

Air locking. The epidural filters commonly used in this country prevent aspiration once the filter is wet if air is present within it. Aspiration can still be achieved if 1.5 ml of saline is first injected through the filter and this will have the additional advantage that any blockage in the epidural catheter will be cleared. Midwives should be taught to perform this test before injecting local anaesthetic top-ups, as many cases of late catheter migration can be detected in this way.[10,24,62]

Incorrect identification of aspirated fluid. Though blood is easy to recognise, CSF can be mistaken for saline injected during localisation of the epidural space. Berry[63] described the use of 'Clinistix' to distinguish between the glucose-containing CSF and normal saline. If this test is used a high rate of false positive responses can be envisaged as blood[63] and saline[64] have both been found to produce blue colouration of these strips. CSF aspiration can only be diagnosed with certainty if more fluid is aspirated than is injected.

Failure of the test dose to predict intravascular injection

Intravascular injection of local anaesthetic occurs for one of four reasons.

Failure to perform an aspiration test.

Inadequate test dose. Local anaesthesia is not an effective indicator of intravascular injection; less than 70% of unpremedicated general surgical patients reported any effects after deliberate intravenous injection of 3 ml of a variety of local anaesthetic solutions, including 1.5% lignocaine and 0.75% bupivacaine.[52] Albright has described cases where 2, 3, 4 and 5 ml test doses of 0.75% bupivacaine failed to indicate intravascular injection, sometimes with fatal consequences.[15,65] Adrenaline must be used in the test dose if there is any risk of convulsion or cardiotoxicity following the therapeutic dose. The only adrenaline test dose that has been fully investigated is a 15 μg injection. This is the dose that should be used.

Misinterpretation of the test dose. In labour, sedation, panic and pain can make interpretation extremely difficult. Nervousness and palpitations, which are felt in 100% of unsedated volunteers given an intravenous injection of 15 μg of adrenaline, are seldom reported in sedated subjects, even on direct questioning.[52] Successful interpretation of the test dose in obstetrics can only be achieved if signs of intravascular and subarachnoid injection are used which do not in any way rely upon patient cooperation.[13,21] Thus, when adrenaline is used, ECG monitoring of the heart rate is mandatory. Intravascular injection is diagnosed if a 20% increase of heart rate occurs within 40 seconds of injection.

Late intravascular catheter migration. (*Table 3*).

Table 3. Catheter migration during obstetric epidurals

Author	Number of cases	Size of series	Number of normal top-ups before complication	Complication	Effect	Comments
Ryan[62]	1	Case report	1	Intravenous catheter migration	Convulsion	Anaesthetist present, full recovery, live baby
Philip and Brown[67]	1	Case report	2	Subarachnoid catheter migration	High spinal block—CSF was freely aspirated from catheter afterwards	Anaesthetist present, full recovery, live baby
Ravindran *et al.*[66]	1	Case report	3	Intravenous catheter migration	Convulsion	Anaesthetist present, full recovery, live baby
Kenepp and Gutsche[22]	12	4003	No details	Intravenous catheter migration	Diagnosed by aspiration of blood before injection	Convulsions occurred in 20% of intravenous catheter migrations
	13				Diagnosed when tremor or convulsion occurred during top-up	No details of maternal or fetal outcome given
Crawford[10]	2	28 000	(a)1, (b)5	Intravenous catheter migration	Total spinal block, cardiac arrest	Anaesthetist delayed by 4 minutes. Mother recovered after 2 days in ITU. Live baby
	1		1	Intrathecal catheter migration		

This is a relatively common occurrence,[22] which is seldom reported unless serious complications occur.[10,62,66] Intravascular migration can often be diagnosed by aspiration,[22] which should be done before every epidural top-up.

Failure of the test dose to predict subarachnoid injection

Once again there are many avoidable factors.

Failure to perform an aspiration test. Having produced a total spinal block, several authors have shown that CSF could be freely aspirated through the epidural catheter.[24,60,67]

Inadequate test dose. Data obtained from studies in general surgical patients have often been used to suggest large volume test doses which are inappropriate in pregnant women.[52] Obstetric anaesthetists have recommended lower volumes and concentrations of local anaesthetic,[31,68] but evidence that these can produce an effective spinal block within 5 minutes is often not available.

Bupivacaine 0.5% is available in both isobaric and hyperbaric solutions and has been used as a spinal anaesthetic solution in pregnancy,[25,30,32] yet it is not always effective as a test dose.[58] Occasionally the block it produces is extremely slow in onset and is missed at 5 minutes.[69] The 0.25% solution is likely to be even less effective and its use is not recommended.

Lignocaine would seem an ideal agent for test doses. It has a very fast onset and a short duration of action, but which preparation should be used? The hyperbaric 5% solution has been recommended,[70] but there are two problems with its use. Firstly, a large dose of local anaesthetic is used; this limits the size of the therapeutic dose and may result in confusion as a significant epidural block may develop within 5 minutes. Secondly, the preparation is not widely available in this country. Lower concentrations (0.5–2%) have gained a reputation for producing an inadequate block intrathecally,[70] but evidence for this is extremely poor.[71,72] One paper has recently shown[73] that a 2-ml test dose of 1.5% lignocaine in 7.5% dextrose with adrenaline is an effective and safe test dose in pregnancy. Following subarachnoid injection, all 15 patients developed an objective sensory block within 2 minutes. In the epidural group, only one out of 250 patients developed objective sensory loss before 4 minutes. Even though the numbers are small, it is clear that this formulation has much to recommend it; however, like the 5% solution it is not at present available in this country.

It is hoped that the manufacturers will make a heavy solution of 1.5% lignocaine available as soon as possible, but until that happens, what is the best alternative? We consider that despite the lack of hard evidence to support its use, 2 ml of 1.5 or 2% plain lignocaine is the drug of choice. Preservative-free lignocaine in these concentrations is widely available in labour wards and it produces a block of rapid onset using a dose which is unlikely to produce an effect if injected epidurally.

Misinterpretation of the test dose. This can be reduced to a minimum only if normal pinprick sensitivity in the lower legs and feet is clearly demonstrated 4 minutes after injection. Motor blockade does not occur until after the development of sensory block and is less useful as an indicator.

Late subdural catheter migration (*Table 3*). This is far less common than intravascular migration,[10] but far more lethal. Three fatalities have occurred in this way since 1984. Aspiration can prevent this complication[67] and midwives should do this before every top-up injection. It is not standard practice to give a test before each top-up at present and it is unlikely that this would be effective as interpretation is complicated by residual blockade.

Recommended safety procedure before epidural injection of local anaesthetic in obstetric patients

Aspiration

An aspiration test should be performed before all epidural local anaesthetic injections.

Epidural pain relief in labour

Total spinal block will occur if the therapeutic dose is injected intrathecally, but convulsions and cardiotoxicity due to intravascular injection have not been reported after doses of less than 25 mg of bupivacaine or 100 mg of lignocaine. A 2-ml test dose of 1.5–2% lignocaine should be given whenever this sort of epidural is set up, but it is not necessary to add adrenaline. All therapeutic injections should be made slowly over 1–2 minutes. If a top-up fails to work the doctor in charge of the epidural must decide between giving an adrenaline test dose or replacing the epidural.

Epidural blockade for operative delivery

If more than 25 mg of bupivacaine or 100 mg of lignocaine is to be used as the therapeutic dose, a test dose of 2 ml of 1.5–2% lignocaine and 15 μg of adrenaline is necessary as both intravascular and subarachnoid injections can be lethal. As there is no solution containing exactly this mixture, we recommend that 3 ml of 1:200 000 adrenaline should be injected first and when the ECG confirms that the drug has not been given intravenously the lignocaine can be given.

Patients with restricted placental blood supply

In patients with pre-eclamptic toxaemia, diabetes, intra-uterine growth retardation or evidence of frank fetal distress, even small intravenous injections of adrenaline can be dangerous to the fetus. If operative delivery is required, adrenaline should be avoided. Epidural blocks using bupivacaine should only be performed if incremental doses of less than 5 ml are administered by slow injection. It may be preferable to use spinal anaesthesia in these patients.

Test dose failure

This protocol will minimise the incidence of accidental total spinal and intravenous injections, but occasional cases will occur. Some will happen when the first dose of local anaesthetic is injected because the test dose has failed to produce an adequate effect or because an inexperienced anaesthetist has failed to assess it correctly. Occasionally accidental total spinal blockade due to late catheter migration will occur. Though uncommon, this possibility has important implications. Deaths from total spinal blockade can be prevented by prompt intubation and resuscitation. Staff who are familiar with these techniques must be available at a moment's notice whenever a local anaesthetic is injected into the epidural space and resuscitation equipment must be available wherever an epidural is performed.

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Anaesthesia, 1986, Volume 41, pages 1251–1254

Forum

Single breath end-tidal PCO$_2$ measurement during high frequency jet ventilation in critical care patients

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Summary

The relationship between arterial and end-tidal carbon dioxide tensions following a single large breath was investigated in seven critically ill patients receiving high frequency jet ventilation. There was a close correlation ($r = 0.989$) between arterial and end-tidal carbon dioxide tensions over a wide range (3.29–8.95 kPa). Measurement of the end-tidal carbon dioxide tension following a single large breath may be useful in monitoring the efficiency of high frequency jet ventilation in the elimination of carbon dioxide.

Key words

Measurement techniques; end-tidal CO$_2$.
Ventilation; high frequency.

The rôle of high frequency jet ventilation in critically ill patients is not yet fully defined.[1-4] The ability of high frequency jet ventilation to maintain adequate gas exchange while high peak airway pressure is avoided may be used to reduce barotrauma,[5,6] ventilate patients with bronchopleural fistula[7,8] and to ventilate neonates with hyaline membrane disease.[9,10] High frequency jet ventilation has also proved to be appropriate in anaesthesia for pulmonary surgery,[11] bronchoscopy, laryngoscopy[12] and neurosurgery.[13,14]

The mechanism of CO$_2$ clearance during high frequency jet ventilation remains unclear. There appears to be a reduction in physiological dead space, an increase in functional residual capacity,[12] and improved gas mixing with augmented diffusion.[1,15] If rapid equilibrium between alveolar CO$_2$ tension and pulmonary capillary CO$_2$ tension occurs, the end-tidal CO$_2$ tension from a single large breath should correlate well with arterial CO$_2$ tension. Measurement of end-tidal CO$_2$ tension following a single large breath has been demonstrated in dogs with normal lungs to reflect accurately the effectiveness of CO$_2$ elimination during high frequency jet ventilation.[16] This study was designed to ascertain whether the single-breath method is also applicable to patients with impaired pulmonary function.

Methods and materials

Seven critically ill patients receiving high frequency jet ventilation were studied. High frequency jet (HFJ) ventilation was indicated because of failure of conventional intermittent positive pressure ventilation to maintain adequate blood gas tensions, difficulty in weaning from conventional ventilation or to avoid high peak airway pressure. High frequency jet ventilation was delivered via a Mallinckrodt Hi Lo double-lumen jet tracheal tube by an HVJ ventilator (Acutronic Mark 800) with heated humidifier.

Ventilatory rates of 100–150 breaths/minute were used, with an inspiratory:expiratory ratio of between 1:2 and 1:1.5. All patients were also connected to the breathing system of a Bear Mark 1 ventilator which delivered a continuous flow of humidified O$_2$ in air at the same concentration as the jet ventilator. This system provided a source of gas for entrainment. Continuous positive airway pressure could be applied via this system and the intermittent mandatory ventilation mode provided a sigh at the rate of 3 times/minute.

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Measurements were made after 30 minutes of high frequency jet ventilation. Changes in ventilation were made only as indicated clinically. Subsequent measurements were made 30 minutes after each change in ventilator setting. Arterial blood was withdrawn from an indwelling radial arterial line for immediate analysis of partial pressures of O_2 and CO_2 by an automatic blood gas analyser (Corning 175). The intrapulmonary shunt fraction was not measured because not all patients had a pulmonary artery catheter *in situ* at the time of the study and it was not considered ethically justifiable to insert one solely for this purpose. Immediately after the arterial sample was taken, the patient was disconnected from the jet ventilator and a single breath of tidal volume 12 ml/kg was delivered from the Bear Mark I ventilator. The end-tidal CO_2 tension was recorded using a capnograph (Gould Mark 4,) attached to the sampling port of the tracheal tube (1.5 cm from the tip of the tracheal tube); the sampled gas was not returned to the system. The peak value was read from a galvonomic scale and digital display, but a trace was not obtainable.

The capnograph was switched on an hour prior to any measurements being made and was calibrated against 5% CO_2 in nitrogen (Engström standard calibration cylinder) before each measurement. The response time was 0.1 seconds. The barometric pressure was measured using a mercury barometer and the CO_2 concentration was converted to partial pressure.

Results

The age, sex, weight and medical condition of the patients are shown in Table 1.

In all patients there was an improvement in arterial O_2 tension following the institution of high frequency jet ventilation, compared with conventional intermittent positive pressure ventilation at the same inspired O_2 concentration and similar levels of continuous positive airways pressure.

Three of the patients studied subsequently died from overwhelming sepsis. In two, the improvement in arterial O_2 tension seen after the institution of high frequency jet ventilation was maintained until death. In the third, the initial improvement in arterial oxygen tension was not maintained, prompting a return to conventional ventilation.

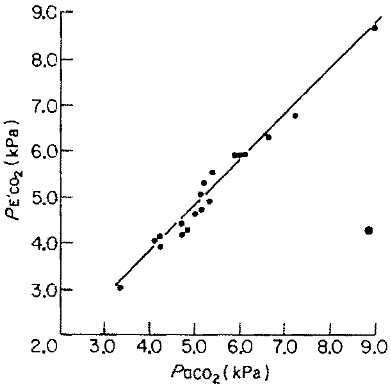

Fig. 1. Relationship between single large breath end-tidal CO_2 tension and arterial CO_2 tension in seven patients receiving high frequency jet ventilation. Correlation coefficient 0.989 (y intercept at -0.236).

The ventilation and the CO_2 tension measurements are shown in Table 2. The arterial and corresponding end-tidal CO_2 measurements are displayed in scattergram form in Fig. 1. There was close agreement between single large breath end-tidal CO_2 tension and arterial CO_2 tension over the range of CO_2 tensions encountered (correlation coefficient 0.989). The regression line was drawn by computer using a general statistics package. Students's paried t-test applied to these results give a probability of <0.0001.

Discussion

High frequency jet ventilation may replace conventional intermittent positive pressure ventilation in

Table 1. Age, sex, weight and medical condition of the subjects of this study

Patient number	Age (years)	Sex	Weight (kg)	Medical condition	Outcome
1	65	M	62.1	Right upper lobectomy, pneumonia.	Recovered
2	87	M	68.4	Multiple injuries, flail chest.	Recovered
3	69	M	73.2	Post cardiac arrest, pneumonia. Chronic obstructive airways disease.	Died
4	62	F	72.5	Partial hepatectomy, pneumonia and septicaemia.	Recovered
5	40	M	74.1	Bacterial endocarditis, septicaemia, prosthetic mitral valve. Left ventricular failure.	Died
6	72	M	72.3	Head injury, aspiration, pneumonia. Barotrauma on intermittent positive pressure ventilation.	Recovered
7	64	M	80.1	Biliary peritonitis, septicaemia. Adult respiratory distress syndrome.	Died

Table 2. End-tidal carbon dioxide tensions and simultaneously measured arterial CO_2 and O_2 tensions

Patient number	$P\mathrm{aCO_2}$ (kPa)	$P\mathrm{E'CO_2}$ (kPa)	$P\mathrm{aO_2}$ (kPa)	$F\mathrm{IO_2}$ (%)	Inspiratory time	CPAP (cm H_2O)	Frequency (breaths/minute)
1	5.92	5.92	13.52	0.75	30%	+10	100
	6.10	5.92	10.17	0.6	30%	+10	100
	7.24	6.84	16.84	0.8	30%	+10	100
2	4.72	4.21	14.71	0.45	40%	+ 5	150
	4.82	4.30	14.63	0.45	40%	+ 5	150
3	4.21	4.09	17.45	1.00	40%	+ 8	150
4	3.29	3.00	23.91	0.8	30%	+ 5	150
	4.09	4.00	16.82	0.6	30%	+ 5	150
	5.20	5.26	11.82	0.5	30%	+ 5	150
	5.13	5.00	12.24	0.4	30%	+ 5	150
5	5.13	4.74	8.89	0.6	30%	+ 5	150
	5.00	4.61	10.01	0.6	40%	+10	150
	6.58	6.31	13.10	0.6	40%	+10	150
	8.95	8.92	8.82	0.4	40%	+ 8	150
	6.05	5.92	10.41	0.6	40%	+ 8	150
6	4.21	3.95	14.75	0.55	40%	+ 6	150
	4.74	4.47	14.64	0.5	40%	+ 6	150
7	5.39	5.51	11.72	0.7	40%	+10	100
	5.26	4.87	10.80	0.7	40%	+10	100

$P\mathrm{aCO_2}$, arterial carbon dioxide tension; $P\mathrm{E'CO_2}$, end-expired CO_2 tension; $P\mathrm{aO_2}$, arterial oxygen tension; $F\mathrm{IO_2}$, fractional inspired oxygen concentration; CPAP, continuous positive airway pressure.

selected critically ill patients[2-4] and during some surgical procedures.[10-12] However, it is difficult to assess the adequacy of CO_2 elimination clinically during high frequency jet ventilation.[17] The preset minute jet flow and entrainment flow do not correspond to the effective minute alveolar ventilation.[18] Routine end-tidal CO_2 tension measurements are not helpful when the tidal volume is less than the anatomical dead space. Regular monitoring of blood gas tensions is usually considered essential during high frequency jet ventilation. A rapid non invasive test that can be performed frequently would be a useful aid to the monitoring of high frequency jet ventilation in an intensive care unit and in the operating theatre as an alternative to frequent arterial blood sampling.

When lung function is normal, end-tidal CO_2 tension corresponds closely to arterial CO_2 tension during intermittent positive pressure ventilation or spontaneous respiration.[19] However, this may not be the case in the presence of pulmonary dysfunction[20,21] and it is perhaps surprising that such a good correlation between end-tidal CO_2 tension and arterial CO_2 tension following a single large breath was found in patients with severe pulmonary dysfunction.

It is possible that the improvement in gas mixing and reduction in dead space that occurs during high frequency jet ventilation may account for the accurate reflection of arterial CO_2 tensions by end-tidal CO_2 tension.

This technique of measuring end-tidal CO_2 following a single large breath is an accurate indicator of arterial CO_2 tension in patients with poor lung function. It is probable that the method would be equally useful in indicating the efficiency of ventilation in patients with normal lungs undergoing high frequency jet ventilation during anaesthesia.

In conclusion, in a small group of critically ill patients receiving high frequency jet ventilation, measurement of end-tidal CO_2 tension following a single large breath did not differ significantly from arterial CO_2 levels measured simultaneously. Single large breath CO_2 measurement may be useful in the routine monitoring of patients receiving high frequency jet ventilation.

Acknowledgments

I am grateful to Dr B.H. Doran, Consultant Anaesthetist and Director of the Intensive Care Unit, Dr N.J.N. Harper, Consultant Anaesthetist and Dr B. Kay, Reader in Anaesthesia for help and encouragement during this study, and to Mr P. Farrow, Intensive Care technician for technical assistance.

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Bent Haxholdt

This a personal tribute to the late Bent Haxholdt, past President of the Danish Society of Anaesthetists, who died on the 31 January, 1986, after a distressing illness. He had been ill for some months, but he continued to work until late in November last year (1985).

Bent Haxholdt was a true friend of many British anaesthetists. He spent a considerable part of his training period in the Department of Anaesthetics in Cardiff and came to this country frequently after his return to Denmark. He was for many years a regular attender at our Association Meetings. He was President of the Danish Society when a joint meeting was held with the Association at the Commonwealth Institute in September 1978 and was awarded the Pask Certificate for his contributions in promoting good relations between our two countries.

Bent was a delightful, friendly man, full of humour and goodwill towards his colleagues. Nothing was too much trouble if he felt he could be of any help to his friends. Any British anaesthetists visiting Copenhagen found him a most generous host and they could rely on him to give every possible assistance during their stay. His charming wife, Olga, also an anaesthetist, was an ideal partner and together they made a splendid ambassadorial team at our meetings. Their many friends in this country mourn the loss of a most distinguished colleague.

Brettes,
Back Lane.
Monks Eleigh.
Suffolk

P.J. HELLIWELL

Halothane hepatitis in a child?

Doctors Whitburn and Sumner (*Anaesthesia* 1986; **41:** 611–3) report a case of halothane hepatitis in a 10-month-old undernourished Asian infant having his third thoracotomy for repair of a recurrent tracheo-oesophageal fistula. Previous surgery included oesophagoscopy, bronchoscopy, jejunostomy and median sternotomy.

There are several potential causes for postoperative jaundice in this infant. The patient probably received multiple blood transfusions so non-A, non-B hepatitis is possible. Currently, over 90% of post-transfusion hepatitis is due to non-A, non-B hepatitis. Hypoxia and hypotension were not recorded in the patient's records. This should not be taken to mean that they did not occur. A 10-month-old infant with chronic aspiration and lung disease having his third thoracotomy would be very likely to sustain episodes of hypoxia, both intra- and postoperatively. Surgical retraction can lead to direct hepatic trauma, hepatic venous congestion and diminished portal and arterial hepatic blood flow; all of these may influence postoperative hepatic function.

A positive diagnosis of halothane hepatitis would be difficult to sustain in the absence of specific halothane-related antibodies. Many serological tests to diagnose halothane hepatitis have been described: lymphocyte stimulation test, the macrophage migration inhibition test, antibodies to halothane altered rat liver membranes, halothane cytotoxicity test using 1,1,1-trichloropropene oxide, blood eosinophilia, liver–kidney microsomal auto-antibodies, antimitochondrial antibodies, raised concentrations of IgE, elevated circulating immune complexes and lowering of the third and fourth component of complement. None of these tests has achieved widespread acceptance.

The authors attribute to the serological test for halothane hepatitis performed at Kings College Hospital a degree of confidence which is not shared by other workers in the field.[1] That the infant developed unexplained hepatitis following surgery and halothane anaesthesia is indisputable. That the hepatic failure was positively diagnosed as halothane hepatitis is conjectural. The avoidance of halothane in a subsequent anaesthetic was prudent and in line with the recommendation of Strunin.[2]

It would have been interesting to compare pre- and postoperative antibody titres. It would also be interesting to know how long this child retains the halothane-related antibody.

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A reply

We agree with Dr Wark that the possibility of non-A, non-B hepatitis must be considered in any case of postoperative jaundice and that its diagnosis is often made by the exclusion of other causes. However, we disagree that the finding of specific halothane antibodies was not, at the very least, suggestive that halothane was the cause of liver failure in the infant we reported and that the presence of such antibodies does not indicate a sensitisation to halothane.[1] Even if this were not so, it stretches the imagination too far to suppose that the timing of the non-A, non-B infection allowed it to appear exactly postoperatively in our patient, or could contribute to unexplained pyrexia and tachycardia seen with previous halothane anaesthetics given for minor surgery.

Of course, halothane is too valuable an agent in paediatric anaesthesia for its use to be abandoned even for repeated usage, but where postoperative jaundice occurs, the possibility that halothane is the causative agent should be borne in mind. We believe that the burden of proof now rests with those who do not believe that halothane causes jaundice even in the occasional child and suggest that Dr Wark may be like the ostrich, burying his head in the sand.

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Absorption of epidural morphine

Widespread initial distribution of morphine in the vessel-rich epidural environment might result in significant vascular uptake. A wide distribution within the epidural space conversely might result in increased penetration by morphine of the dura and binding to the spinal cord over a considerable segmental range. Both mechanisms could influence the quality of analgesia, perhaps in opposite directions.

In an attempt to evaluate this effect, patients who were undergoing cholecystectomy received a constant dose of epidural morphine in two different volumes. Morphine plasma levels were assayed and pain scores determined. The study was approxed by the ethics committee of the hospital and the patients gave their informed consent. Two, approximately similar, groups of patients randomly received either 6 mg preservative-free morphine hydrochloride in 3 ml or the same dose in 30 ml. The epidural injection was made at the T_{9-10} level before induction of anaesthesia. The drugs used for premedication, and general anaesthesia, including muscle relaxants, were identical in the two groups.

Venous blood samples for plasma morphine assays, using high pressure liquid chromatography, were drawn at 0, 5, 10, 15, 30 and 60 minutes after the epidural injection.[1] Intensity of pain was assessed by a consultant, who was not aware to which group the patient belonged. A visual analogue scale (0–10 cm) was used at one and 3 hours postoperatively, capillary

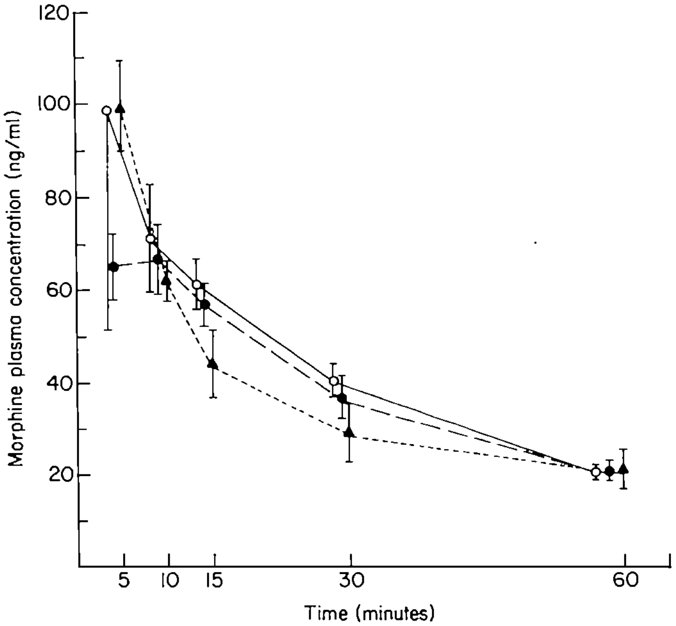

Fig. 1. Plasma concentrations in the three groups of patients. ○, Morphine 6 mg in 3 ml; ●, morphine 6 mg in 3 ml epidurally; ▲, morphine 6 mg in 3 ml intravenously.

blood gas analysis was performed at one and 6–8 hours postoperatively and respiratory rates were measured at 15–30 minute intervals until at least 12 hours had elapsed from the epidural injection. The time until first request of additional analgesic, the number of requests and possible side effects were recorded. An additional group of four patients were given 6 mg of morphine intravenously and the plasma concentrations were assayed at the same intervals as above.

There were no significant differences in the plasma concentrations of morphine between the three groups (Fig. 1), which suggests that the vascular uptake of morphine from the epidural space is quite rapid and that possibly most of the morphine dose is absorbed before the dural transfer. This confirms the results of an earlier study in patients with choledochal drainage (T-drain), which showed that even low doses of epidural morphine began to raise the intracholedochal pressure within a few minutes.[2] In the 30-ml group there were large interindividual differences in morphine concentrations at 5 and 10 minutes, probably reflecting the anatomical variability of the epidural space. The patient with the highest morphine concentration, 376 ng/ml at 5 minutes, needed no additional medication during the first 24 hours and was walking the following morning. Since, we assume, much of the epidural morphine dose was lost into the systemic circulation, unsatisfactory analgesia would have been expected.

The analgesia provided by the 30-ml solution seemed to last somewhat longer than that by the 3-ml dose. There were no requests for analgesics in the first 2 hours in the 30-ml group and three out of seven patients required no additional analgesics in the 24-hour postoperative period. All six patients in the 3-ml group needed supplementary analgesics, four of them within the first 2 hours. The mean pain intensity was low: the mean value was 2 in the 30-ml group (range 0–6) and 3 in the 3-ml group (range 1–6). Cutaneous hypoalgesia, which was tested by pinprick at one and 3 hours, was observed at the midthoracic area in four patients of the 30-ml group, but in one of the 3-ml group.

None of the patients had severe respiratory depression. However, all of the epidurally treated patients (four men, nine women) had urinary retention during the first 24 hours. This side effect, which may respond to naloxone,[3] prompted us to discontinue the study.

In conclusion, there seems to be no difference in the absorption of morphine from the epidural space, regardless of the volume used. Postoperative analgesia was slightly better with the 30-ml volume, perhaps, due to a wide area of binding of morphine to the spinal cord.

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Hypothermia and multiple sclerosis

Mild depression of body temperature by 0.7 °C is known to cause transient improvement of the symptoms and signs of multiple sclerosis.[1] The long term sequelae of deep hypothermia associated with coronary artery bypass surgery in such patients are unknown.

A 62-year-old man with paraplegia subsequent to a 15-year history of multiple sclerosis presented for coronary artery grafting. He had developed ischaemic pain at rest following two subendocardial myocardial infarcts 2 months prior to admission. Previous inguinal herniorrhaphy and general anaesthesia had led to an exacerbation of his multiple sclerosis, manifested by transient weakness of his left arm. Two other operations under general anaesthesia had resulted in no neurological deterioration.

Medication on admission included atenolol 25 mg bd, perhexilene 100 mg bd, diltiazem 120 mg tds, diazepam 2.5 mg tds, glyceryl trinitrate paste, amoxicillin 250 mg tds, frusemide 40 mg daily and oral potassium supplementation. Significant neurological findings consisted of slightly diminished power in the right arm, absent power in the lower limbs and decreased sensation in all modalities below T_{10}. Cardiorespiratory examination was unremarkable apart from bilateral basal inspiratory crepitations.

The premedication of papaveretum 20 mg and hyoscine 0.4 mg intramuscularly one hour before insertion of monitoring catheters was supplemented by incremental doses of diazepam 7.5 mg intravenously during placement of pulmonary and radial artery catheters. Other monitoring consisted of ECG and a nasopharyngeal temperature probe. Induction of anaesthesia was attained with phenoperidine 4 mg, alcuronium 20 mg and intermittent positive pressure ventilation of the lungs with 60% nitrous oxide in oxygen. Saphenous vein grafting to the left anterior descending and right coronary arteries was uneventful. The patient was cooled during this procedure to 27 °C when cardiopulmonary bypass commenced and rewarmed to 37 °C before weaning from the pump.

His progress was complicated 3 days postoperatively when he developed an exacerbation of upper limb weakness, the right being more affected than the left. This weakness coincided with a lower urinary tract infection and associated pyrexia of 39 °C. Removal of his indwelling urethral catheter and antibiotics led to a resolution of his temperature. Three weeks postoperatively he had regained his pre-operative levels of function.

Deep induced hypothermia led to no exacerbation of the signs or symptoms of multiple sclerosis. Transient postoperative neurological deterioration was associated with a known aetiology—pyrexia.[2] Other possible sources of upper limb weakness such as over vigorous sternal retraction[3] or traumatic cannulation of the right internal jugular vein[4] may be excluded because of the late onset and relatively short episode of exacerbation of the limb weakness.

Coronary artery bypass grafting should be offered to patients with ischaemic heart disease who would normally warrant it. Some have been excluded in the past because of concern over the possible consequences of marked hypothermia and cardiopulmonary bypass on their multiple sclerosis. Avoidance of postoperative temperature elevation should be energetically pursued.

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Cell-saver

Dr Kumar's letter, (*Anaesthesia* 1986; **41:** 774–5) was interesting. The Haemonetic Cell-saver is a type of autotransfusion blood salvage unit which is not really suitable for very rapid, massive blood loss. It is what I consider to be a slow autotransfusion technique. Other slow techniques are the Receptal system (Abbott Laboratories, Queenborough, Kent) and the Solcotrans (Cabot Ltd, High Wycombe). These techniques are useful when the blood loss is slow enough to be replaced by crystalloid or plasma substitutes. However, the Cell-saver produces the highest quality salvaged red cells and one can, of course, also recover other cellular components. Really large, rapid blood loss can only be salvaged and replaced immediately using the Bentley ATS system (Bentley Laboratories, Ilford), which uses a roller pump or a similar device[1] made up of standard cardiothoracic unit supplies. Very large blood loss of several litres/minute can be recovered and immediately replaced with this roller pump system. It has the disadvantage, as does the Cell-saver, that it requires technical personnel to run it safely. It does, however, have the advantage that since the blood is salvaged immediately from the wound and passed straight back to the patient in a closed loop, Jehovah's Witness patients often accept this form of autotransfusion rather than others which involve some break in the loop.

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Lack of haematological and biochemical consequences following autologous blood transfusion

The use of autologous blood transfusion during surgical operations is becoming established practice when major haemorrhage is expected. This technique is useful when stored blood is difficult to obtain because of shortage, incompatibility or rapidity of the bleeding; it may also diminish the risk of viral cross infection. Various authors have reported on the efficiency of such methods as the red cell-washing[1] (Cell-saver, Haemonetics, Natick, MA, USA), whole blood recycling systems[2] (the Sorenson receptal device, Sorenson Research Corporation, Salt Lake City, Utah, USA) and the autotransfusion system[1] (Bentley Laboratories, Irvine, CA, USA).

We have been using an automatic system (Haemonetics Cell-saver) during liver transplantation which, following the collection of blood from the operative field, heparinises it, then separates the red blood cells by centrifugation, washes and resuspends them in saline with a haematocrit of 60%.[1]

There is controversy in the literature over the existence[3] or not[4] of a coagulopathy due to heparin which is re-infused with activated clotting factors. Any abnormalities that do exist should be particularly apparent in patients following liver transplantation in whom impaired liver function limits the body's ability to inactivate heparin and activated clotting factors. Liver function is impaired during liver transplantation, at the beginning when the recipient's own liver is being skeletonised, during the anhepatic phase and for several days after re-implantation of the donor liver when recovery from the ischaemic damage sustained when the liver was extracorporeal, occurs. Haemorrhage can occur intra-operatively during all of these phases, due to adhesions following previous surgery or division of anastomotic vessels. Bleeding is exacerbated by the portal hypertension and coagulopathy. In addition, the infusion of large amounts of washed red cells suspended in 0.9% saline may lead to biochemical abnormalities such as hypernatraemia and hypokalaemia.

The intra-operative biochemical and haematological changes of cell-saving systems[5] and liver transplantation[6] have been described separately, but little attention has been given to postoperative effects. Blood loss and administration details of 20 patients are shown in Table 1.

Immediately on admission to the intensive care unit after liver transplantation routine investigations are performed on arterial blood (Table 2). The patients had all received a similar amount of stored (citrate, phosphate, dextrose and adenine) blood intra-operatively. Ten of these patients had received, *in addition*, between 0.67 and 4.3 litres of cell-saved red blood cells. No statistically significant differences were found between any haematological or biochemical variables between the two groups (Student's *t*-test).

Table 1. Blood loss and administration details in ten patients who received banked blood only and ten patients who received banked blood and cell-saved blood.

	Cell-saved group mean value (SD) (litres)	Non cell-saved group mean value (SD) (litres)
Total blood loss	7.4(4.09)	4.5 (1.77)
Total transfusion (banked + cell-saved)	7.88 (3.08)	6.25 (1.32)
Banked blood	6.23 (2.63)	6.25 (1.32)
Cell-saved red blood cells	1.65 (range 0.67–4.3)	Nil

Table 2. Investigations performed on the two patient groups.

Investigation	Cell-saved group mean value (SD)	Non cell-saved group mean value (SD)
Biochemical		
Hydrogen ion (mmol/litre)	36.4 (5.95)	34.2 (4.91)
Base excess (mmol/litre)	2.7 (4.79)	2.3 (5.09)
Potassium ion (mmol/litre)	3.2 (0.48)	3.0 (0.52)
Sodium ion (mmol/litre)	136 (3.59)	137 (4.07)
Glucose (mmol/litre)	20.7 (9.86)	14.7 (7.22)
Urea (mmol/litre)	9.8 (7.06)	6.0 (3.64)
Haematological		
Haemoglobin (g/dlitre)	13.8 (1.59)	13.4 (2.28)
Platelets ($\times 10^{-9}$/litre)	116 (54.49)	181 (85.43)
Prothrombin time ratios*	1.47 (0.19)	1.37 (0.15)
Partial thromboplastin time ratios*	1.45 (0.50)	1.15 (0.08)
Thrombin time ratios*	1.24 (0.15)	1.12 (0.14)

* Patient/control.

The use of a red cell washing and re-infusion system of this type appears not to cause significant haematological or biochemical disturbances in patients following liver transplantation. It is therefore unlikely to cause significant changes in other groups of patients.

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Safety hazard with cylinder yoke on a Boyle's machine

The following incident occurred recently and could have led to injury. A BOC International Mk 2 anaesthetic machine was in use, working from cylinders. One of the oxygen cylinders, having nearly emptied, was changed for a fresh one. This was offered up to the yoke, the retaining bar was swung into place and the winged screw tightened in the usual way.

The cylinder valve was opened to check the pressure of the contents whereupon there was a sudden escape of gas at high pressure from between the valve and

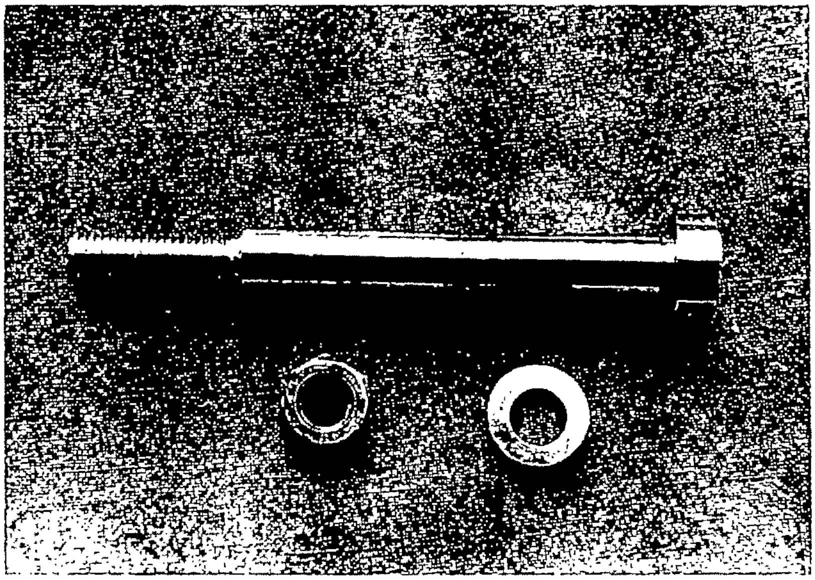

Fig. 1.

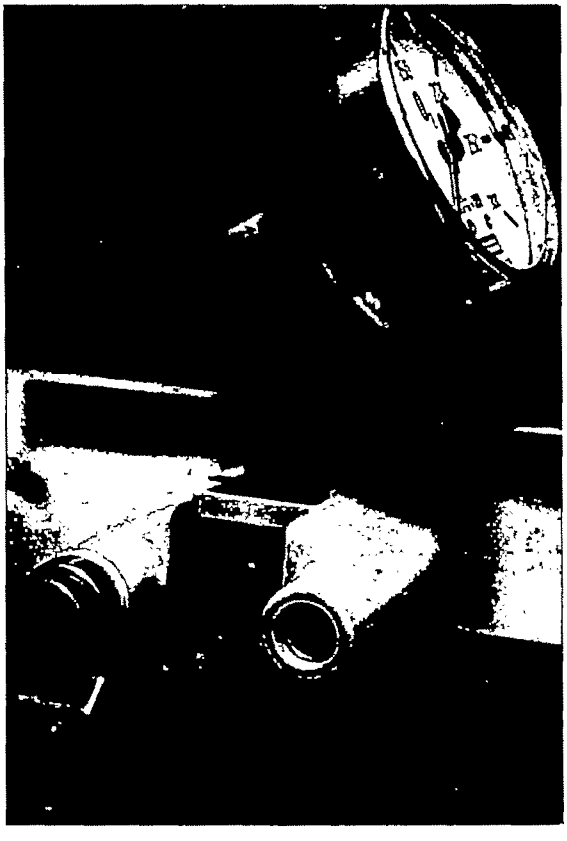

Fig. 2.

yoke. One of the nursing staff closed the valve promptly. The cylinder remained attached to the yoke. Examination revealed that one of the bolts (Fig. 1) which fix the yoke to the side-member of the machine was loose. This had permitted the retaining bar and screw to move slightly away from the machine, thus allowing the cylinder to blow away from the Badock seal on the yoke. The cylinder was only just hanging on the pins of the pin index. It was found after removal that the right-hand bolt was loose and could be completely removed, without any rotation (Fig. 2).

The nut and washer which normally hold the bolt through the yoke and side-member of the machine were found soon afterwards on the floor. There was no evidence of damage to the thread of the bolt. It is presumed that the nut had worked loose, but that the bolt had somehow become fixed in the hole (perhaps with the washer jammed between a thread and the back of the side-member), so that the cylinder was held in place with no apparent problem. Movement which occurred when the cylinder valve was opened finally loosened the bolt, leading to the events described.

The nut and washer are of a simple design with no obvious means to prevent them from working loose. The yoke is the only means of support for the cylinder, so perhaps a locking nut (e.g. 'Nyloc'), or nonslip washer, might prevent a similar occurrence. No harm occurred on this occasion, but it caused considerable alarm amongst the theatre staff, including those operating at the time; if the cylinder had become dislodged only a little more it could have dropped to the floor with dangerous results.

The machine was subsequently examined and reassembled by a BOC engineer before being brought back into service.

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Epidural test doses

We would like to comment on the recent letters concerning epidural test doses that appeared in your columns. We agree absolutely with the general points made by Dr Crawford (*Anaesthesia* 1986; **41:** 766) of the pitfalls of overreliance on test doses, but suggest that there are occasions when even anaesthetists who do not usually employ a test dose may wish to reassure themselves that all is well with the catheter. The important point is to use a single dose that will rapidly demonstrate either subarachnoid or intravenous injection, without causing harm to the patient.

In a recent study we compared plain bupivacaine 0.5% and lignocaine 2% for spinal anaesthesia and found that, while the solutions produced blocks of similar extent, the onset was much faster with lignocaine.[1] All the patients who received 4 ml lignocaine 2% had both subjective and objective signs of profound block at the first (2-minute) assessment. With 4 ml bupivacaine 0.5% (the test dose advocated by Dr Wilton, *Anaesthesia* 1986: **41:** 765) several patients had quite minimal evidence of block at this time. We would therefore suggest that 4 ml lignocaine 2% is more appropriate for rapid identification of subarachnoid injection. In our experience of patients with chronic pain, this dose of lignocaine (80 mg) almost always produces transient but mild symptoms when injected intravenously.

Whether this dose of lignocaine is considered to be a test dose or a fraction of a therapeutic dose is immaterial. We believe that it gives the greatest chance of detecting problems and avoiding disaster. No test dose can guarantee the latter and we support Dr Crawford's policy of slow, fractional injection of the main dose.[2]

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Long-term ketamine infusion

A 19-year-old man was involved in a car crash. He sustained a head injury, a haemopneumothorax, a fractured pelvis and a torn perineum, leaving a gaping wound. The patient was transferred to our unit for dialysis because of renal failure. The chest and head injury quickly resolved. A Hoffman apparatus was used to stabilise the fractured pelvis and a fluidised bed to help nursing care.

Pain relief presented enormous problems because morphine infusion was insufficient to meet the need and an epidural was considered to be unsafe because of local sepsis and the need for regular haemodialysis.

A ketamine infusion was therefore used in view of the reports of postoperative pain relief[1–5] and its value in asthma;[6] the latter was a persistent problem after the patient's trachea was extubated.

The ketamine was made up as a 0.1% solution, diluted in 5% dextrose and delivered by a syringe pump. The dose varied between 0.2 and 0.8 mg/kg/hour, titrated to clinical requirements; at the upper end of the dose range the patient became unrousable but over the next 36 hours he settled at 0.3 mg/kg/hour without cardiovascular or respiratory problems and was easily rousable. A total of 4318 mg was administered in all. The infusion was stopped on day 7, since it was noted that the patient was becoming increasingly withdrawn and less communicative. There were no emotional sequelae and thereafter only very occasional analgesia was necessary. The patient also had ten consecutive ketamine anaesthetics (50–150 mg) for changes of the perineal pack over the next 4 weeks without any problems.

The use of ketamine in this way is not yet approved by licence, although it is known to be useful as an infusion for analgesia. We are unable to find any other reported case of a ketamine infusion used in this situation and consider that such a technique may be beneficial in similar clinical situations.

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Bain anaesthetic system and gender

It is generally agreed that the use of the Bain anaesthetic system enables normocapnia to be maintained during surgery in most patients, provided fresh gas flow ($\dot{V}_{FG}$) and minute ventilation ($\dot{V}_E$) are set to 70 ml/kg/minute and 140–150 ml/kg/minute, respectively.[1] However, it is our experience that when these values are used, moderate to severe hyperventilation may result.

A systematic study of intra-operative carbon dioxide tension ($Pa\mathrm{CO}_2$) was performed in 178 consecutive unselected patients who were undergoing elective general surgery. Mean age was 55.2 years (SD 17.2). Premedication and anaesthetic technique were chosen by the anaesthetist in charge, according to the needs of the patient. On the other hand, the same ventilatory rules were applied to all patients, namely $\dot{V}_{FG}$ 70 ml/kg/minute, $\dot{V}_E$ 140–150 ml/kg/minute, respiratory rate 12 breaths/minute and inspiration:expiration ratio (I:E) = 1:2. All ventilators (Penlon 200) were checked monthly by hospital technicians for accuracy.

A slight degree of hyperventilation was observed in the group as a whole ($Pa\mathrm{CO}_2$ 4.45 kPa, SD 0.62). When patients were divided into two groups according to gender, the women had a significantly ($p < 0.05$) lower $Pa\mathrm{CO}_2$ in all age groups than the men: 4.18 (SD 0.60) and 4.75 kPa (SD 0.5) respectively. This has been noted without comment by others.[2,3] There was no significant dependence on age for men (or for women) (Table 1). The reasons for these observed differences between men and women are not immediately apparent. Metabolic production of carbon dioxide during anaesthesia may depend on the anaesthetic techniques in use. If alveolar ventilation is fixed on a weight basis, as it was in our patients, any differences in $Pa\mathrm{CO}_2$ may be at least in part due to anaesthetic technique *per se*, rather than to the mode of ventilation. However, this was not the case in our patients, because different anaesthetic techniques (e.g. nitrous oxide and oxygen supplemented by fentanyl or other analgesics; enflurane, isoflurane) were equally distributed between sexes. Moreover, Bain and Spoerel found that carbon dioxide production was not statistically different among patients anaesthetised using three different techniques.[3] Finally, it must be remembered that the figures suggested by Bain and Spoerel[1] do not refer to any particular technique of anaesthesia. Dead space[4] and CO_2 production[5] are reported to be less in females than in males and this could explain our findings. The

Table 1. Mean (SD) intra-operative $Pa\mathrm{CO}_2$ and age; differences are not statistically significant intra-group.

Age (years)	<20	21–40	41–60	>60
Males (n = 85)	5.56 (1.29)	4.93 (0.50)	4.80 (0.50)	4.63 (0.41)
Females* (n = 93)	4.53 (0.93)	4.20 (0.41)	4.23 (0.64)	4.04 (0.57)

* $p < 0.05$ (males versus females).

independence of $Pa\text{CO}_2$ of age may be ascribed to the age-related antagonistic changes in carbon dioxide production and respiratory dead space, since smaller respiratory dead space and higher levels of carbon dioxide production characterise young people, compared to those of older subjects.

Our results seem to indicate that any future evaluation of the Bain anaesthetic system and, possibly, any anaesthetic system must take into account the gender of the patients under study. Meanwhile, a slight reduction of $\dot{V}_{FG}$ in females ventilated by the Bain system seems desirable. Arterial blood gas analysis is however advisable whenever a fine-tuning regulation of $Pa\text{CO}_2$ is mandatory (neurosurgery).

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Emergency guided blind intubation

The principle of retrograde tracheal intubation via an existing tracheostomy was established in 1960 by Butler and Cirillo,[1] and was subsequently modified by Waters using cricothyroid puncture.[2] There have since been further modifications of this technique using extra catheters[3] and Seldinger wires.[4]

The classical technique has disadvantages in an emergency. It is time consuming and also involves considerable manipulation within the airway, such that oxygenation may be impaired. The Mini-tracheostomy kit[5] (Portex Ltd, Hythe) can be used as an emergency airway for cases of upper airway obstruction. It also comes complete with a stiff plastic introducer which may be used in a retrograde fashion for guided blind tracheal intubation.

Cricothyrotomy is performed with the guarded scalpel provided in the kit. If the patient is *in extremis*, or if conventional bag and mask ventilation is inadequate, the minitracheostomy tube may be inserted and used to gain access to the lower airways for resuscitation. When oxygenation is satisfactory, the introducing stylet may be inserted in a retrograde manner into the oropharynx using, if necessary, a second cricoid puncture. A well-lubricated tracheal tube is then introduced via the mouth or nose and advanced over the stylet with the aid of Magill's forceps. When the tracheal tube abuts against the anterior wall of the trachea, the stylet may be gently withdrawn. Axial pressure is maintained on the proximal end of the tracheal tube to prevent it slipping into the oesophagus. With the stylet removed, continued pressure will cause the tracheal tube to slide down into its correct position.

This technique was used successfully in four cases of unexpected difficulty with tracheal intubation. When intubation is expected to be difficult, techniques using awake intubation under local anaesthesia are preferable.[6]

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Training in fibreoptic intubation

Most anaesthetists have little experience of fibreoptic intubation,[1] but it is probably the method of choice in the management of many difficult airways. Confidence is best gained on patients with normal anatomy. Few would wish to be intubated awake, yet this has been described as part of a training programme in fibreoptic nasotracheal intubation.[2] We prefer such training to take place during the course of routine general anaesthesia.

To this end we regularly perform fibreoptic nasal intubation on patients who present for minor oral surgery. We use a simple technique which, with two anaesthetists, need not prolong the operating list. Anaesthesia is induced, with a suitable intravenous agent while the previous case is still on the table, and continued with oxygen, nitrous oxide and halothane breathed spontaneously until sufficiently deep to allow the nose to be sprayed with up to 10% cocaine 2 ml and the larynx with 4% lignocaine 2 ml. After a period of breathing halothane in oxygen only, but maintaining deep anaesthesia, the patient is ready to be intubated. Both anaesthetists must be present at this stage. One holds the tongue forwards, ensures a clear airway and thus provides an unhurried opportunity for the operator to perform the fibreoptic endoscopy and intubation before the patient becomes too light.

There is little risk of hypoxia as one anaesthetist carefully monitors respiration throughout. Modified airways and masks[3] are not needed. We use an anaesthetic technique for minor oral surgery which includes halothane and spontaneous respiration, but we have seen strikingly few ventricular dysrhythmias. The reasons for this are not clear. We also avoid any morbidity associated with suxamethonium. Little unnecessary delay is incurred by overlapping cases with two anaesthetists.

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Anaesthesia and gastric carcinoid

We welcome the opportunity to report a case which presents a few interesting and unusual features in addition to those recently reported.[1,2]

A 41-year-old female presented as emergency with severe diarrhoea, vomiting, sweating and facial flushing. She was known to the hospital as having benign gastric carcinoid, diagnosed endoscopically and had suffered from intermittent abdominal symptoms for 3 years. Her urinary 5 hydroxy indole acetic acid levels had always been normal; however, tests had shown antibodies to gastric parietal cells and a low serum B_{12}. She had been maintained on hydroxycobalamin. Liver ultrasound showed two possible deposits in the right lobe.

Laparotomy and gastrectomy were undertaken. One day pre-operatively oral treatment with ranitidine 150 mg tds and cyproheptadine 4 mg tds was commenced. Methylprednisolone 1g was given 7 hours pre-operatively and again one hour pre-operatively; the second dose was given with 200 000 units of aprotinin and premedication with temazepam 20 mg, hyoscine 0.3 mg and promethazine 25 mg. Induction was with droperidol 5 mg, alfentanil 1 mg, midazolam 10 mg and etomidate 20 mg. Tracheal intubation was performed after vecuronium which was also used intermittently to a total dose of 16 mg. Analgesia was with levorphanol 4 mg and maintenance of anaesthesia was with nitrous oxide, oxygen and halothane and intermittent positive pressure ventilation of the lungs.

The liver was found to be macroscopically normal and a total gastrectomy was performed; the stomach contained benign carcinoid tissue, confirmed histologically.

Remarkable cardiovascular stability was maintained throughout, with one small increase in systolic blood pressure from 130 mmHg to 150 mmHg and pulse rate from 90 to 95 beats/minute during handling of the tumour. Postoperative recovery was uneventful.

The rationale for management was as follows. The likeliest hormones in foregut tumours are histamine and bradykinin. Ranitidine was given for H_2-blocking effects and has been shown to be as effective as H_1 and H_2 combinations. Aprotinin is a kallikrein trypsin inhibitor and blocks the formation of bradykinin. Methyl prednisolone blocks synthesis of prostaglandin, which may be released from the tumour and which also takes part in the action of bradykinin. Cyproheptadine was given for its antiserotonin effects as, despite this being a foregut tumour, diarrhoea, which is usually a serotonin effect, was present.

The most unusual feature of this case was the occurrence of the carcinoid syndrome, which normally requires metastasis to the liver, in a patient with benign tumour.[3] One can only postulate that there was sufficient systemic venous drainage of the stomach to allow the short acting peptides to bypass the liver.

It is also gratifying that an uneventful course was obtained with this regimen, although this has obviously been achieved with other techniques by various workers.

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Severe hypoxaemia during cardiopulmonary bypass

This is a case of severe hypoxaemia during cardiopulmonary bypass (CPB) caused, we consider, by the misplacement of the gas-mixing sponge in the oxygenator; this resulted in inefficient gas exchange, unresponsive to increases in gas flow.

An asymptomatic 20 kg, 7-year-old Chinese boy was scheduled for repair of a secundum type atrial septal defect (ASD), which had been confirmed by angiography. Premedication consisted of trimeprazine, morphine and hyoscine. Anaesthesia was induced with etomidate, pancuronium and fentanyl. Maintenance was with a ketamine infusion and the lungs were ventilated with 100% oxygen. An increment of pancuronium was given when cardiopulmonary bypass (CPB) was established. The aorta was cross-clamped and the heart arrested, as the patient was cooled to 32°C.

The blood which was leaving the oxygenator was noted to be dark soon after the right atrium was opened (Table 1, sample 2). The oxygen flow was increased to 3, then 4 litres/minute, with no improvement in the hypoxaemia (sample 3). A mixed venous sample at this time did not indicate excessive oxygen extraction.

The ASD and atriotomy were quickly closed and ventilation restarted with 100% oxygen, the heart was

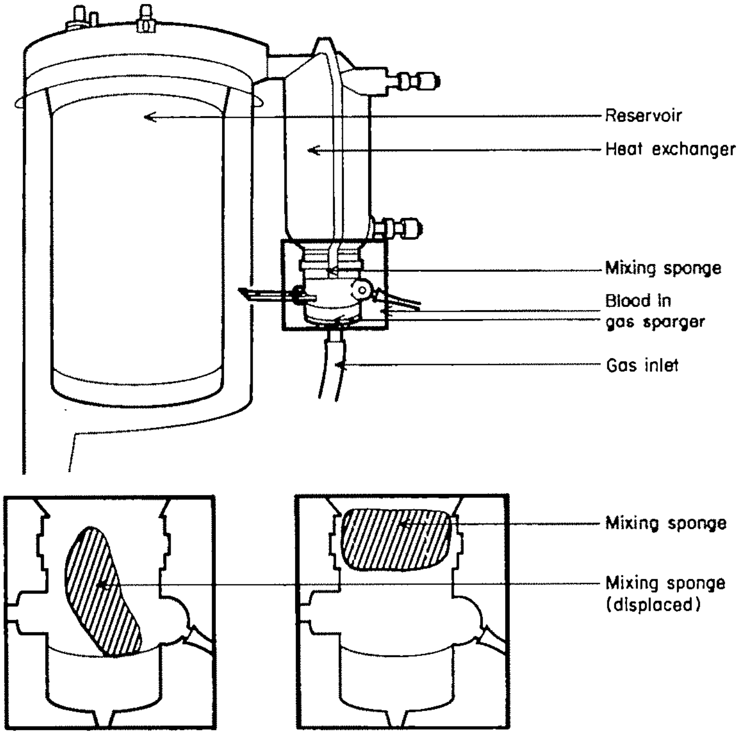

Fig. 1.

Table 1.

		pH	$P\text{ao}_2$ (kPa)	$P\text{aco}_2$ (kPa)	Base excess mmol/litre
Sample 1	Before CPB	7.46	60.1	4.4	+0.2
Sample 2	6 minutes CPB	7.41	4.8	5.4	+1.9
Sample 3	11 minutes CPB	7.41	4.5	5.4	+2.8
Sample 4	20 minutes CPB	7.52	58.6	4.3	+6.1

de-aired and the aortic clamp removed. The hypoxeamia rapidly resolved as the heart began to eject (sample 4). Weaning from bypass and the remainder of the operation were uneventful. Elective postoperative ventilation of the lungs was started. The patient's trachea was extubated when he was fully conscious and his cardiovascular system stable, 18 hours later. No neurological defect was detected postoperatively.

The oxygenator was examined at the end of CPB and the position of the mixing sponge was discovered to be as shown in Fig. 1. The Shiley 070/S oxygenator is a very efficient gas exchange unit. This efficiency is due to the presence of the mixing sponge.[1] The gas is dispersed into the blood through a gas sparger and optimal conditions for gas transfer are created by passing the mixture through the open porous mixing sponge.

This incident caused considerably greater hypoxaemia than those cases reported by Gravlee, Wong and Charles[2] and was unresponsive to increases in the gas flow. Alternative causes for hypoxia on CPB are inadequate oxygen flow reaching the oxygenator, hypoxaemia caused by channelling of blood within an oxygenator, when blood flow exceeds the limits of the oxygenator's capabilities, excessive haemodilution, hyperthermia and thrombosis within the oxygenator.[3] None of these causes was applicable in this case.

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Intensive care for Legionnaire's disease

The case report by Power and Bowen (*Anaesthesia* 1986; **41:** 620) was interesting but disappointing because the management of the patient was not described in more detail. There are some aspects which need further explanation.

It is stated that severe hypoxia was present prior to elective ventilation of the lungs; the $P\text{ao}_2$ was 6.9 kPa with the patient breathing from an MC mask with an oxygen flow of 8 litres/minute. It is also stated that an $F\text{io}_2$ 0.6 and positive end expiratory pressure (PEEP, 0.5 kPa) were required to achieve a $P\text{ao}_2$ of 7 kPa. Perhaps I am being particularly obtuse, but it appears to me that the original severe hypoxia was little improved by the procedure of tracheal intubation and ventilation. Later in the report, it is stated that there was no arterial hypoxaemia at any time. If this was indeed the case, would the authors explain how they achieved this in the face of the severe shunt ($>30\%$) that was present. Did they increase the $F\text{io}_2$, the level of PEEP, or both, and did they encounter any problems as a consequence?

Later in the report, the authors describe episodes of supraventricular tachycardia with severe haemodynamic instability and state that this is not widely recognised as a common complication (of *Legionella* pneumonia?). They do not, however, make any mention of the treatment of these episodes. Supraventricular tachydysrhythmias are, in fact, relatively common in the critically ill patient and although many can be explained by such things as disordered electrolytes, hypoxia, myocardial infarction or pulmonary embolus, there are a large number which cannot be adequately explained and which occur during episodes of fever, sepsis or sympathetic stumulation.[2] Conventionally, such dysrhythmias have been treated with digoxin or beta-blockers, but more recently verapamil has been found to be very useful in this context.[3] Indeed, when a high degree of sympathetic stimulation is present, as in most forms of stress, this is a logical drug to use and there have been some recent reports of its highly successful administration as an infusion. Any negative inotropic effects of this drug may be easily reversed by intravenous calcium and it appears that this has no effect on its antidysrhythmic properties.[4]

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Dr Power and Dr Bowen describe an interesting case of atypical pneumonia in which there was a delay in identification of the causative organism, although it was suspected on clinical grounds (*Anaesthesia* 1986; **41:** 620–2). In their discussion they do not mention the possibility that tuberculosis might cause a similar clinical picture. We are at present preparing a manuscript about a previously fit Caucasian young woman who developed miliary tuberculosis and required an extended period of mechanical ventilation (42 days). The diagnosis was initially uncertain and an atypical pneumonia was suspected. However, after extensive investigation *Mycobacterium tuberculosis* was isolated.

Acid alcohol fast bacilli (AAFB) were not present at first in sputum, urine or gastric washings, but were identified in tissue taken at transbronchial and liver biopsy. Failing early demonstration of AAFB using routine noninvasive techniques, rapid diagnosis may be made by transbronchial biopsy and/or bronchial brushings, biopsy of liver, bone marrow or any clinically enlarged organ.[1] Bone marrow trephine has a higher yield than aspiration.[2]

There are many reported cases of miliary tuberculosis presenting as atypical pneumonia and progressing to adult respiratory distress syndrome and posing a diagnostic problem.[3–5] In some necropsy series, the presence of tuberculosis was unsuspected antemortem in 70–100% of cases.[6] Our case stresses the need for extensive and sometimes invasive investigations to identify or exclude the presence of AAFB in a case of atypical pneumonia when the identity of the causal organism is not rapidly established.

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A reply

Thank you for allowing us to reply. We apologise for any ambiguity regarding the time course of events and the use of the phrase 'at any stage'. On admission, the patient was severely ill and septic and at this time the tachydysrhythmias described could readily be attributed to hypoxaemia and the nonspecific effects of sepsis. Subsequent tracheal intubation and intermittent positive pressure ventilation of his lungs initially did little to improve the $P\mathrm{ao}_2$. Indeed, some 30 days passed before $P\mathrm{ao}_2$ values were achieved which were consistently above 10 kPa. During this period the $F\mathrm{io}_2$ was 0.6 and positive end expiratory pressure (PEEP) varied between 0.5 and 0.8 kPa. This level of PEEP was generally well tolerated without cardiovascular deterioration. Subsequently, $P\mathrm{ao}_2$ values improved, but what prompted our curiosity in this case was that further episodes of supraventricular tachycardia continued to occur following long periods of stability when the arterial oxygen tension was normal. We agree that verapamil is the drug of first choice and it was used in this patient. The point about calcium is interesting, although in this case inotropic support, when required, was provided by dopamine or a combination of dopamine and dobutamine.

Dr Isaac is quite right to state that tuberculosis must always be considered in the differential diagnosis of pneumonia. Appropriate noninvasive investigations for tuberculosis were carried out in our patient until the rising antibody titre to *Legionella pneumophilia* established the diagnosis. We are not competent to comment on transbronchial lung biopsy, but note that even in expert hands the mortality rate after this procedure is 0.12% whilst the incidence of major complications is 2.7%.[1]

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Reference

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Narcotic overdose and acute rhabdomyolysis

The report by Dr Pfeifer (*Anaesthesia* 1986; **41:** 614–9) concerning acute rhabdomyolysis prompts us to describe a case of methadone overdose that was complicated by this unusual condition.

A 27-year-old black male was admitted to casualty, having been found unconscious in a locked room which belonged to a known drug abuser. No history was immediately available. He was noted on admission to be unrousable, with irregular, shallow breathing. He was pyrexial (38.5°C) and hypotensive (70/50 mmHg), with a tachycardia of 108 beats/minute. Discrete haemorrhagic skin lesions were present over the chest wall, the shoulders and the legs. Neurological examination demonstrated pin-point pupils, asymmetrical reflexes and mild neck stiffness.

The differential diagnosis was considered to be narcotic overdose, meningitis or intracranial haemorrhage. The administration of intravenous naloxone 0.8 mg produced no change in the level of consciousness or of pupillary size. Examination of the cerebrospinal fluid showed no abnormality and computerised tomography of the brain was unremarkable. Routine haematological and biochemical investigations were normal and sickle cell status was negative. Resuscitation with intravenous fluids was effected on arrival in casualty and this resulted in an immediate increase in blood pressure and a decrease in pulse rate. The patient's trachea was intubated and his lungs ventilated.

He was admitted to the intensive care unit and his bladder was catheterised; this produced a small volume of dark urine with a specific gravity of 1020. Despite apparently adequate hydration, his urine output averaged only 12 ml/hour during the next 4 hours. The serum potassium rose from 4.2 mmol/litre on admission to 6.7 mmol/litre 5 hours later. Urine osmolality was found to be 292 mosm/litre and a diagnosis of acute renal failure was made. Following a lack of response to the administration of frusemide 250 mg, intravenous fluid was restricted and the patient placed on a dextrose–insulin infusion, which controlled the serum potassium at a level below 6.0 mmol/litre. A blood and urine drug screen revealed the presence of methadone and his creatine phosphokinase (CPK) level was 31 500 units (normal up to 175 units). Subsequent urine electrophoresis demonstrated a myoglobin band. It was concluded that the renal failure was secondary to acute rhabdomyolysis. The patient underwent haemodialysis for 5 days, after which his urinary output increased; his CPK level fell to 4060 units. He proceeded to make a full recovery.

Acute rhabdomyolysis has been reported following prolonged coma and drug overdose. A number of narcotic drugs have been implicated including heroin, methadone and codeine.[1] It is unclear whether rhabdomyolysis is the result of prolonged postural muscle compression or a direct effect of the drug.[2] It has been suggested that prompt diagnosis and treatment of acute renal failure due to rhabdomyolysis may influence the course of the renal failure.[3] Therefore, although acute rhabdomyolysis appears to be an uncommon condition, we suggest that the diagnosis should be borne in mind when acute renal failure following drug overdose is investigated.

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Removal of inhaled peanut using a fibreoptic bronchoscope

A 41-year-old woman presented with a 4-week history of cough and chest infection after an episode of flicking peanuts into the air and catching them by mouth at Christmas. She was otherwise well, apart from gross obesity; she weighed 102 kg.

She had been admitted several days after the suspected inhalation. Rigid bronchoscopy had failed to show any foreign body, although the procedure was foreshortened by an episode of cyanosis and apparent bronchospasm. Intermittent suxamethonium was used during the anaesthetic and a Sander's injector was employed for ventilation of her lungs. The left bronchial tree and the right main bronchus had been visualised by the time the procedure was abandoned.

She was readmitted 4 weeks after the suspected inhalation with the symptoms of unresolved right basal pneumonia despite antibiotic therapy. She was presented for diagnostic fibreoptic bronchoscopy under general anaesthetic. A number of additional items were available for possible use.

An ECG monitor was connected and the patient was anaesthetised with gallamine 20 mg pretreatment and thiopentone induction; a size 9.0 cuffed tracheal tube was passed using suxamethonium 150 mg. Anaesthesia was maintained with intermittent positive pressure ventilation of the lungs with nitrous oxide in oxygen and trichloroethylene 0.2%. Relaxation was maintained with incremental doses of suxamethonium. The flexible

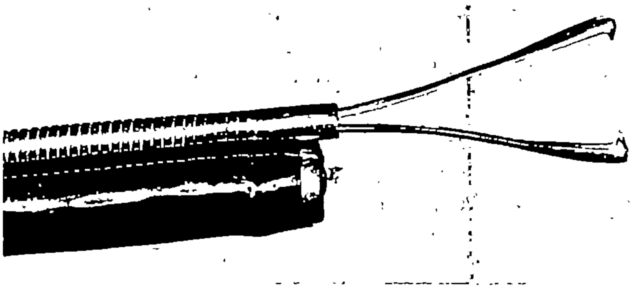

Fig. 1. Colonoscope biopsy forceps attached to bronchoscope.

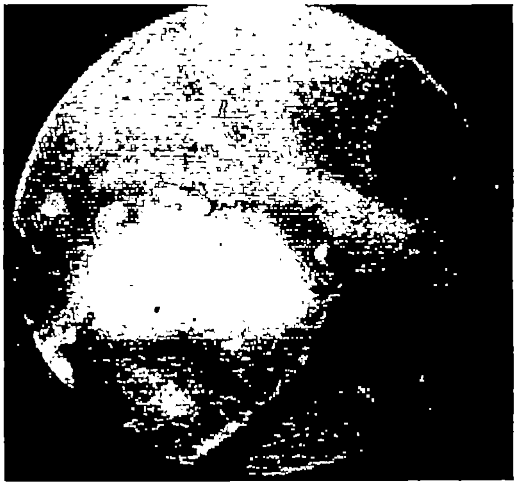

Fig. 2. Peanut being grasped by forceps.

bronchoscope was passed through the diaphram of the Portex swivel connector. A hard white foreign body was seen beyond the origin of the right lower lobe.

A dormier basket was tied, using strong silk, to the outside of a second bronchoscope with the basket slightly beyond the tip. The peanut was dislodged with this. A colonoscope biopsy forceps was then secured in a similar manner to the first bronchoscope (Fig. 1) and the peanut was eventually grasped and carefully withdrawn; the Portex swivel connector was removed when the peanut was in the tracheal tube. The patient was kept apnoeic at this stage to reduce the chance of losing the peanut again. A small remaining fragment was removed by holding it onto the tip of the bronchoscope by suction. The two fragments made up a complete peanut cotyledon.

Anaesthesia was difficult because of the high inflation pressures needed as a result of the presence of the bronchoscope, a large leak around the tracheal tube, because of the additional equipment, the patient's obesity and the need to keep the patient apnoeic at times. One hundred percent oxygen and manual ventilation of the lungs was needed at critical stages. The whole procedure took 20 minutes, during which a total of 400 mg of suxamethonium was used.

The patient rapidly regained consciousness and full muscle power and made an uneventful recovery. The potential for a thoracotomy to remove the foreign body was thus avoided by a little ingenuity and some patience. We have not heard of any other reported cases of removal of inhaled peanut by flexible bronchoscope.

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Visual confirmation of correct positioning of double lumen tubes?

Drs Rocke, MacGillivray and Mahomedy's letter (*Anaesthesia* 1986; **41:** 770–1) about checking correct placement of double lumen tubes with a fibreoptic bronchoscope was interesting. It proved impossible to pass our Olympus BF 10 fibreoptic bronchoscope down the largest size Bronchocath. Perhaps they have a smaller diameter scope?

Assuming that they possess a bronchoscope able to pass down the available double lumen tubes, I fail to see how it is then possible to direct the end of the bronchoscope to look through the aperture in the right-sided Robertshaw tube to confirm that it is directly over the right upper lobe bronchus. Perhaps a right-angled viewing bronchoscope telescope could be introduced through the double lumen tube, in order to view correct positioning of the tube aperture over the right upper lobe bronchus, but would the pre-formed shape of double lumen tubes allow this? If Dr Rocke *et al.* are speaking from practical experience, it would be valuable to learn their technique of visual confirmation that the placement of bronchial tubes is correct.

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Equipment malfunction: possible hazard

A Fluotec Mark III vaporizer was recently found to be delivering no halothane at any setting and, as usual, this discovery was made inadvertently and at a most inconvenient moment. The Fluotec was on a Selectatec mounting and was easily withdrawn from service. Messrs Ohmeda at Keighley dismantled the vaporizer and reported that from the serial number on the case, this was a device that they had sold to another manufacturer of anaesthetic equipment some 4 years ago; it appeared that somebody other than an Ohmeda or Cyprane technician had been tinkering with it because a nonstandard screw had been used to close the cover plate. The Woodruff key was entirely missing, so that turning the setting spindle had absolutely no effect (luckily, ours was set to zero, otherwise it could have been fixed at 4% and the vaporizer would deliver high concentrations, no matter what the setting). The service date, obliterated on the metal foil label attached to the vaporizer, was 3 years overdue. Finally, in addition to the failure of our programme of phased servicing, it had never been officially organised, so that we were paying the most expensive fee!

This experience brought home the importance of observing the servicing dates and the desirability of buying vaporizers direct from the maker, for there is no product liability attaching to the equipment of one firm that has been mounted on the machinery of another or that has passed through other hands before reaching the ultimate user. It is another argument in favour of committing all the anaesthetic equipment in one theatre to one maker; product liability is thereby preserved.

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A reply

Dr Duncan's letter highlights the difficulties that can occur when a service policy of cure rather than prevention is followed. Our service policy on vaporizers has always been that prevention is preferable to cure. Hence, we recommend a thorough annual overhaul, during which a full review of all mechanical parts is undertaken, all seals and wicks are replaced and calibration is checked.

This is a policy which we support wherever our products are used. To this end we have established a global network of over 40 service centres, whose technicians are trained to high technical standards and capable of performing service to standards equivalent to those at our factory.

We would certainly endorse Dr Duncan's view that purchasing decisions on equipment should take into account the servicing capabilities of the supplier, particularly where that equipment has an important life support function.

Regarding Dr Duncan's point on product liability, it is not strictly correct to say that in the case of components or distribution of products that product liability would not extend up the supply chain to the manufacturer. Product liability is a question of proof of negligence and it is a matter of law and fact as to where negligence occurred in the supply chain.

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Herpes simplex after spinal pethidine

The efficiency of spinal opioids in relieving both visceral and somatic pain is tempered by documentation of a number of side effects such as pruritus, nausea and vomiting, urinary retention and respiratory depression.[1] Dr E. Cardan (*Anaesthesia* 1984; **39**: 1031) called attention to activation of *herpes simplex* as another possible side effect of spinal morphine in 7–14 year-old enuretic children.

Such a herpetic lesion located on the lower lip and recognised by the dermatologist as oral shedding of herpes simplex virus type I (HSV) was noted by us in a 21-year-old girl who received 35 mg 5% pethidine hydrochloride, injected intrathecally[2,3] in order to obtain a saddle block suitable for incision of a perineal abscess. The herpetic eruption emerged after 4 days of neurological complaints which started 24 hours after subarachnoid puncture. Lumbar puncture was performed at L_{4-5} with a 22-gauge needle. The next day the patient complained of backache around the site of puncture; this later spread upwards and was followed by a postural headache and photophobia. Neurological examination showed nuchal rigidity. The retinal arterial pressure was 25 mmHg. All the complaints subsided after 4 days of abundant hydration with saline solutions, but the patient had an attack of migraine and developed the herpetic eruption. Revision of her past history revealed that she was hypotensive (with a retinal arterial pressure of 15 mmHg) and suffered from recurrent migraine.

It is well known that HSV infection remains latent, as shown by the ability to isolate the virus from sensory ganglia.[4] Each clinical manifestation is the outcome of virus release from these sites. Pethidine, as well as morphine, can reach sensory ganglia as a consequence of its rostral spread in the cerebrospinal fluid (CSF). However, there are a variety of other factors which could contribute to HSV reactivation; among them, surgical intervention, lumbar puncture[5] and emotional stress[6] may have been contributory in our case. The delayed activation of HSV shedding, after 4 days of complaints was assumed to be due to a decline in the CSF pressure and suggests that the leakage of liquor into the epidural space could be responsible for the HSV reactivation. It is difficult to be certain that this was the cause, or whether pethidine was acting as an irritant.[7] In any case, the reactivation of HSV in our patient could be assessed as a complication of spinal anaesthesia and analgesia.

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Forensic anaesthesia

Law suits against doctors in general, and anaesthetists in particular, are not everyday occurrences, at least in the Third World countries. Nonetheless Forensic Medicine forms an integral part of the undergraduate medical curriculum. Anaesthetists need more that just a working knowledge of the medicolegal aspects of anaesthesia, which may aptly be termed 'forensic anaesthesia'.

The basis of this opinion springs from the environment in which an anaesthetist works: a poor doctor–patient relationship is sometimes observed during the pre-, and postoperative period; the bulk of an anaesthetist's work is done while the patient is not aware; this work involves the use of a number of machines, gadgets, electrical, and electronic equipment about which the anaesthetist may not have complete knowledge, and the maintenance of which may not be directly under his care; the smoothness of an anaesthetist's work depends, to some extent at least, on the competence of the technicians working under his guidance.

It is, therefore, proposed that a formal course in forensic anaesthesia should be included in the period of training/residency programme. The actual laws are different in different countries, but the broad and basic principles could be covered. The help of a lawyer would be valuable in planning. Knowledge about the law would encourage appropriate confidence in the event of an anaesthetic accident or a malpractice suit brought on behalf of an innocent patient. In many centres anaesthesia technicians undergo a formal training programme; they are therefore expected to be under an obligation to carry out their work properly.

Anaesthetists should be aware of some of the Latin terms used in law since these may alter their expectations of their technicians, and *vice versa*. *Respondeat superior*, for example, means let the superior give answer; the responsibility of a principal for his agents' act and the power of control, is the test of liability under the doctrine of *respondeat superior*.

Res ipsa loquitur is well known to mean that a thing speaks for itself, but also a case in which mere proof that an accident took place is sufficient under the circumstances to warrant an inference that it was caused by defendant's negligence unless otherwise explained.

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Induction of anaesthesia in children

Dr Jago's recommendation (*Anaesthesia* 1986; **41:** 885) that intramuscular ketamine be used to induce anaesthesia in the totally uncooperative child concurs with my own former practice. However, ketamine administration is associated with an incidence of psychological disturbance in children as in adults, though possibly less frequently. There may also be excessive salivation in an unpremedicated child.

Intramuscular methohexitone (6–8 mg/kg, 4 or 5% solution) is a very satisfactory alternative, which does not have the same potential disadvantages. It is no more painful on injection than ketamine and takes only a few minutes to become effective. The mode of administration is not new, having been described some 25 years ago.

This technique is usually reserved for those rare occasions when relatively urgent surgery is required for a distraught and uncooperative youngster. However, one little girl aged 3, hated needles and feared the gas, yet needed anaesthesia repeated at weekly intervals as part of the management of her leukaemia. She was found to accept intramuscular methohexitone reasonably cheerfully. Local complications such as induration or pain at the site of injection were repeatedly looked for but never found.

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Further errors with intrathecal morphine

The report of Dr Pomonis *et al.* on overdosage of intrathecal morphine is very interesting (*Anaesthesia* 1986; **41:** 670; note should also be taken of the Erratum Statement, page 1083). The letter graphically illustrates the effects of dilutional errors when dealing with intrathecal opiates, and I suggest that the exclusive use of specifically formulated morphine for intrathecal administration at a concentration of one mg/ml or less may help to prevent a repeat of these potentially life-threatening errors.

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Barnet General Hospital intensive care unit and the Barnet ventilator

A meeting was held over a year ago to celebrate the 20th anniversary of our unit. The occasion was marked by the presentation to the hospital of the original prototype of the Barnet ventilator, which is now displayed at the Medical Centre. It was presented by Mrs Barbara Rochford whose husband, the late James Rochford, FFARCS, had been the principal founder of the unit. This machine (see Fig. 1) was made in 1955 and bears a remarkable resemblance to some more modern ventilators. It has been restored and refurbished by Dr R.F. Welch, FRC Path, the original designer of the machine, together with Mr D.P. Winks, who is still Senior Chief MLSO at the hospital.

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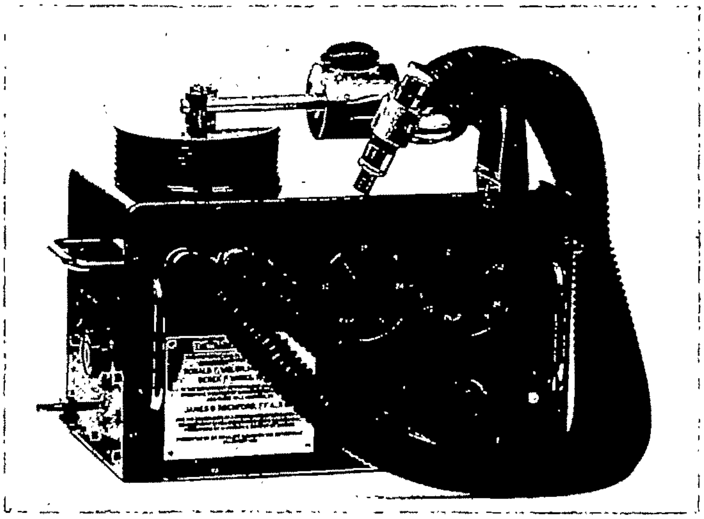

Fig. 1. Prototype 'minute volume divider' lung ventilator made at Barnet General Hospital in 1955.

Anaesthesia, 1986, Volume 41, pages 1274–1276

Book reviews

Anesthetic Managment of Difficult and Routine Pediatric Patients 1274
Edited by F.A. Berry
Anesthesia and the Geriatric Patient 1275
Edited by S.W. Krechel
Ventilators. Theory and Clinical Application 1275
Y.G. Dupuis
Noninvasive Respiratory Monitoring 1276
Edited by M.L. Nochomovitz and N.S. Cherniack

Anesthetic Management of Difficult and Routine Pediatric Patients

Edited by F.A. Berry. Pp. 462, Churchill Livingstone, 1986. £33.00.

It was not long ago that there was a dearth of textbooks on paediatric anaesthesia. However, suddenly, a number of well known paediatric anaesthetists have edited texts on this important and developing specialty. This is of relevance not only to the anaesthetist in training in paediatric specialist hospitals, but of vital importance to those working in general hospitals, since it is estimated that up to 70% of all anaesthetics for children aged between 1 month and 3 years are administered in district general hospitals in the United Kingdom. Similar figures may well apply to many other countries which do not have a large number of specialised children's hospitals.

This textbook is edited by Dr Frederic Berry and written mostly by members of the University of Virginia Medical Center, particularly by those from the Children's Medical Center. Dr Berry is the main contributor for over half of the contents and the opinions given obviously reflect many of his own personal preferences. The book is intended for anaesthesia residents or practising anaesthesiologists and is intended to provide information in controversial areas with less detail than Gregory's recent two-volume *Pediatric Anesthesia* and more explanation than Steward's *Manual of Pediatric Anesthesia.*

There are fifteen chapters in the book and the titles express the editor's concern over aspects of anaesthesia, in its widest sense, that are not universally accepted and are therefore controversial. Like every other specialty, there are a number of different and acceptable variations in technique for providing safe anaesthesia in children, although it is becoming increasingly obvious that basic approaches are converging rather than diverging. Thus, tracheal intubation and controlled ventilation using muscle relaxants are increasingly recommended, even from conservative centres, based upon sound physiological and anatomical principles.

Topics that excite the most interest are, rightly, the emphasis on airway problems. Thus, 208 pages are devoted to anesthesia for the child with a difficult airway, negative pressure pulmonary edema, paediatric bronchoscopy, bronchography and laryngoscopy, acute airway obstruction with special emphasis on epiglottitis and croup, the child with asthma and the child with the runny nose. This last chapter occupies 20 pages and is thought by the editor to be 'one of the enigmas of pediatric anesthesia'. Not all anaesthetists concerned with children might regard this problem with the sincerity of Dr Berry. The initial chapters are concerned with a short history of paediatric anaesthesia, followed by a general philosophy of paediatric anaesthesia, basic considerations and practical aspects of fluid and electrolyte therapy.

The increasing success of the neonatal intensive care units with the survival of extremely low birth weight infants has considerably widened the scope of the neonatal anaesthetist and many more problems are being encountered. A chapter on the anesthetic management of the premature nursery graduate is therefore an important contribution and draws attention to these many difficulties and suggests solutions to these problems.

The place of regional anaesthesia in providing postoperative analgesia is now well established; the chapter on this topic tries to impress those dealing with infants and children with the need for adequate postoperative analgesia for their patients. Techniques for providing pain relief in the wards, apart from the use of morphine in the recovery room, are not discussed, but perhaps this reflects the current role of the paediatric anaesthetist in the United States of America. The importance of the recovery room is indicated by an appropriate chapter and its role is rightly emphasised. Certainly until recently, this topic has not received the attention it deserves in UK practice and all operating theatres need to have suitably equipped and staffed recovery areas. No book on paediatric anaesthesia would be complete without a chapter on malignant hyperthermia and readers will not be disappointed.

This book does not set out to be a comprehensive text of paediatric anaesthesia, but can be recommended to those who feel they require more information, particularly on the practical aspects of certain problems that confront the occasional paediatric anaesthetist.

G.H. Bush

Anesthesia and the Geriatric Patient

Edited by S.W. Krechel. Pp. 252, Grune and Stratton Inc., 1984. £7.84.

The anaesthetic care of the elderly has been unduly neglected as a special interest for far too long. One leading textbook of anaesthesia at least has no chapter devoted to this subject and surprisingly little research work in the field has been published.

British population statistics show a tripling of the proportion of the population aged over 65 during this century and the upward trend continues. Moreover, the aged require far more frequent surgical intervention than others and there is a widening demand for such newer operations as joint replacement and carotid endarterectomy. Certainly any new entrant to anaesthesia can expect to spend a far greater proportion of his time in the management of these patients than was the case with his predecessors.

The importance of this field was recognised early in the Department of Anesthesiology of Washington University School of Medicine (which is, of course, in St Louis, Missouri) and which has organised an annual symposium on the subject since 1974. The work reviewed, edited by Susan Wilson Krechel, consists of sixteen chapters by eighteen contributors and was inspired by these symposia.

The first five chapters deal with the physiology of the ageing process and the changes which occur in the nervous, cardiovascular and respiratory systems, the preoperative assessment of patients and a valuable review of psychological aspects. They set out the present state of knowledge as fully as most anaesthetists will require.

The following three chapters deal with pharmacology. The review of pharmacokinetics and pharmacodynamics is confined to benzodiazepines, thiopentone, the strong analgesics, the older muscle relaxants, atropine and adrenergic agents. It makes clear that there is room for much further and more detailed research. Moreover, the material is largely reduplicated, often in fuller detail and on further drugs, in the chapter on intravenous agents. It is noteworthy that neither atracurium nor vecuronium, which are establishing a major role in the British management of older patients, receives mention in this book. In between the above two chapters is a valuable one on the changes the ageing process brings in the uptake, distribution and actions of volatile anaesthetic agents.

The second half of the book moves on to clinical matters. There are chapters on monitoring, a useful review of pacemakers and ones on the more relevant specialised surgical fields. The value of the latter to the reader will depend on his familiarity and experience in them already. The chapter on anaesthesia for the stroke prone patient is particularly thought provoking. The book ends with an analysis by Professor C. R. Stephen of the risks of anaesthesia and surgery in the geriatric patient and the conclusion that there are no universal ground rules, but each patient must receive individual assessment.

Like most such edited works by multiple authors, the quality and clarity of the presentations by different contributors, the amount of detail contained and the degree of empathy engendered in an individual reader are fairly variable. An excellent and uniform feature, however, is the extensive list of references given to each subject. Certainly this is a work which should be in all Departmental libraries. British readers will be interested to compare it with a more recently published work in the field, which has a single author, a paperback cover, a somewhat different approach and a native origin.

B.H. Smith

Ventilators. Theory and Clinical Application

By Y.G. Dupuis. Pp. 593, C.V. Mosby Co., 1986. £29.00.

The first intermittent positive pressure ventilators to be used in European Respiratory or Intensive Care Units were relatively simple devices which were designed to provide controlled ventilation over a limited range of frequencies. In the United States, however, ventilators designed for inhalational therapy (mainly Birds or Bennetts) were adapted for intensive care use so that the assist mode with pressure cycling became the norm. The relative complexity of the latter machine and the greater proportional involvement of surgeons and physicians in intensive care led to the emergence of inhalation therapists who gradually assumed control of all the technical aspects of respiratory therapy. The service provided by these departments generated an increasing proportion of hospital income. This, in turn, led to increasing expenditure and more and more complex machines which now dominate the market. A similar trend has recently become evident in Europe, so few doctors now have a thorough understanding of the characteristics of the machines they use.

The present volume is written by a respiratory therapist and describes the mechanics and functional characteristics of most of the ventilators commonly used in the United States, though a few (Servo 900c, Engström 300, and Erica) originate from Europe. The text is divided into seven sections. The first provides a very basic review of aspects of respiratory and cardiovascular physiology relevant to mechanical ventilation and a simple description of the various ventilator drive mechanisms. Sections 2 to 5 deal with the factors governing the characteristics of the inspiratory and expiratory phases and with the changeover from inspiration to expiration, and *vice versa.* Section 6 provides a detailed description of thirteen adult ventilators, whilst section 7 deals with five neonatal and paediatric ventilators.

The classification of ventilator mechanisms used in Sections 2 to 5 is firmly based on the work of Mapleson. The functional characteristics of each mechanism are clearly explained with the aid of excellent diagrams, pressure flow and volume traces and simple numerical examples. The diagrams of the ventilator mechanisms are carefully simplified to illustrate the relevant portion of text and are not merely reproductions from manufacturers' literature. An excellent review of the various methods of increasing end-expiratory lung volume in both adult and paediatric practice is also included. These sections provide a comprehensive description of the basic principles underlying the design of mechanical ventilators and would prove comprehensible to any doctor, nurse or technician who is concerned with the use of ventilators. Each chapter has a reaonably comprehensive list of references up to 1983. Sections 6 and 7 describe the design and performance characteristics of individual ventilators. Again, the textual descriptions are clear and the diagrams profuse. Photographs of each ventilator and diagrams of the control panels are included, but there are no pressure, flow or volume traces to illustrate the deficiencies in performance of individual machines. Some of the ventilators described are extremely complex and it is not surprising that these sections are less successful than the rest of the book. Nevertheless, the author has made a good attempt to overcome the problems of explaining the mechanisms to the uninitiated.

This book is obviously aimed at respiratory therapists. It contains no details of clinical practice and there are no critical comments on the performance of individual ventilators. Although it is heavily orientated towards machines used in the United States, it contains a clear description of the fundamental mechanisms used in ventilator design and, as such, would prove valuable to those working in intensive care units in Europe.

M.K. Sykes

Noninvasive Respiratory Monitoring

Edited by M.L. Nochomovitz and N.S. Cherniack. Pp. 229, Churchill Livingstone, 1986. £30.00.

This book was planned to provide a concise review of techniques for noninvasive evaluation of the respiratory system. The editors have collected together a group of experts who have reviewed a range of topics, the majority of which are of great interest to anaesthetists. The result is a series of well written, clearly illustrated and exhaustively referenced chapters which were a delight to read. The opening chapter describes transcutaneous monitoring of oxygen and carbon dioxide. This is the best and most lucid review that I have seen on this subject and it is ideal for examination candidates and research workers in giving a historical review as well as refreshing insights into new applications of this technique. The chapter on oximetry provides a good working account of all the currently available instruments and their uses. This technique is now very widely used in routine anaesthetic practice in North America and is even creeping into UK practice, albeit at a snail's pace. The penultimate chapter on expired CO_2 is a curious offering with a heavy historical bias, little indication of the clinical necessity of measuring expired CO_2 and ignores the use of expired CO_2 measurements in anaesthetic practice. From an anaesthetist's point of view this is the most disappointing chapter in the book.

Between these extremes there are excellent chapters on lung mechanics, chest wall movement, use of ultrasound and CT scanning. The chapter on mechanics is very useful in placing particular emphasis on simple measurements which lend themselves to routine clinical use. This is particularly well illustrated with simple diagrams and uncomplicated mathematics. However, the section on forced airflow oscillation for measuring airway resistance ignores the important advances that have been made in the UK, where the technique has been considerably developed to study the effects on the airways of a range of anaesthetic agents. Despite this lapse the chapter is very good value. There are excellent accounts of methods for measuring respiratory movement using inductance plethysmography and its clinical applications. These represent ideal techniques for the postoperative respiratory monitoring of various analgesic regimens. Of relevance to anaesthetists with intensive care interests are chapters on the evaluation of respiratory muscle function and the assessment of the patient with suspected venous thrombo-embolism. It remains to be seen if the former technique will be clinically useful; nevertheless, the chapter presents a range of techniques ready for further clinical evaluation. A major omission from this book is a description of techniques now widely used for noninvasive evaluation of alveolar capillary permeability relevant to respiratory distress syndromes of both the infant and adult variety. Nevertheless, this is a first rate, slim volume, which I recommend to all anaesthetists contemplating a research project in respiratory function.

J.G. Jones

Anaesthesia, 1986, Volume 41, pages 1277–1284

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This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for June 1986. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

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Errata

Anaesthesia, 1986, Volume 41, pages 829–837

Nikolai Ivanovich Pirogoff

O. SECHER

The first sentence of the last paragraph on p. 831 should read as follows:

He started his investigations on ether early in 1847 and first gave ether by inhalation to a patient on the 14th February.

Anaesthesia, 1986, Volume 41, page 1170

Book review

Cardiovascular Actions of Anesthetics and Drugs used in Anesthesia edited by B.M. ALTURA and S. HALEVY

The publishers regret that, owing to printer's error, the final paragraph of this review by Professor M.D.A. Vickers appeared incorrectly. The final paragraph should read as follows:

Anyone with a high respect for the English language should be warned that it is particularly unsuitable for them. One author tells us that 'the rapid advance in the research laboratory . . . has resulted *literally* (my italics) in an explosion of information'. Some authors give us what they call their 'Future thoughts', most give us boring or ill-constructed sentences. Fortunately, most of them appear to be able at least to write better than the editors whose Preface actually starts with a sentence which uses a singular subject and a plural verb. Let us hope for better things from Volume two.

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Corporate author
The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.
Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)
OSLER AG. *Complement: mechanisms and functions*. New York: Prentice-Hall, 1976.

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American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author
RHODES AJ, VAN ROOYEN CE, *comps. Textbook of virology; for students and practitioners of medicine and other health sciences*. 5th ed. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book
WEINSTEIN L, SWARTZ MN Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: WB Saunders, 1974: 457–72.

Agency publication
National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, Md: National Center for Health Statistics, 1972. (*Vital and health statistics. Series* **10:** Data drom the National Health Survey, No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

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